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DATE: Tuesday, February 19, 2008

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<input type="checkbox"/>	L7	(glycoprotein or glycosylt\$4) and L5	39
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<input type="checkbox"/>	L5	express\$4 same L4	102
<input type="checkbox"/>	L4	(gene or sequence or polynucleotide or cone or recombinant) same L1	322
<input type="checkbox"/>	L3	(gene or sequence or polynucleotide or cone or recombinant) same L2	10
<input type="checkbox"/>	L2	(chondroitinase with glycoprotein)	53
<input type="checkbox"/>	L1	chondroitinase	1496

END OF SEARCH HISTORY

=> index bioscience medicine

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 08:28:42 ON 19 FEB 2008

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=> S chondroitinase

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L1 QUE CHONDROITINASE

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L2 12364 L1

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8 FILES SEARCHED...  
L3 897 (GENE OR SEQUENCE OR POLYNUCLEOTIDE OR CONE OR RECOMBINANT) (S)  
L2

=> S express? (s) L3  
13 FILES SEARCHED...  
L4 308 EXPRESS? (S) L3

=> S (glycoprotein or glycosylt?)(s) L4  
L5 28 (GLYCOPROTEIN OR GLYCOSYLT?)(S) L4

=> S PNGase and L5  
L6 1 PNGASE AND L5

=> dup rem L5  
PROCESSING COMPLETED FOR L5  
L7 16 DUP REM L5 (12 DUPLICATES REMOVED)



=> d ibib abs L7 1-16

L7 ANSWER 1 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2007:257307 USPATFULL <<LOGINID::20080219>>

TITLE: Method for Treating or Inhibiting the Effects of  
Injuries or Diseases that Result in Neuronal  
Degeneration

INVENTOR(S): Eisenbach-Schwartz, Michal, Rehovot, ISRAEL  
Lider, Ofer, Kfar Bilu Bet, ISRAEL  
Rolls, Asya, Rehovot, ISRAEL  
Cahalon, Liora, Givatiam, ISRAEL

NUMBER KIND DATE

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PATENT INFORMATION: US 2007225251 AI 20070927  
APPLICATION INFO.: US 2004-570989 AI 20040908 (10)  
WO 2004-US29288 20040908  
20061227 PCT 371 date

NUMBER DATE

-----  
PRIORITY INFORMATION: US 2003-60500690 20030908  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW,  
SUITE 300, WASHINGTON, DC, 20001-5303, US  
NUMBER OF CLAIMS: 20  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 10 Drawing Page(s)  
LINE COUNT: 1972  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Oligosaccharides, and in particular disaccharides, which are degradation  
products of chondroitin sulfate proteoglycan are effective for use in  
treating, inhibiting, or ameliorating the effects of injuries or  
diseases or disorders that result in or are caused by neuronal  
degeneration or of disorders resulting in mental and cognitive  
dysfunction.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2007:120920 USPATFULL <<LOGINID::20080219>>

TITLE: Primers for synthesizing full-length cDNA and their use

INVENTOR(S): Ota, Toshio, Fujisawa-shi, JAPAN

Isogai, Takao, Inashiki-gun, JAPAN  
Nishikawa, Tetsuo, Tokyo, JAPAN  
Hayashi, Koji, Ichihara-shi, JAPAN  
Saito, Kaoru, Kisarazu-shi, JAPAN  
Yamamoto, Junichi, Kisarazu-shi, JAPAN  
Ishii, Shizuko, Kisarazu-shi, JAPAN  
Sugiyama, Tomoyasu, Kisarazu-shi, JAPAN  
Wakamatsu, Ai, Kisarazu-shi, JAPAN  
Nagai, Keiichi, Tokyo, JAPAN  
Otsuki, Tetsuji, Kisarazu-shi, JAPAN

PATENT ASSIGNEE(S): RESEARCH ASSOCIATION FOR BIOTECHNOLOGY (non-U.S.  
corporation)

NUMBER KIND DATE

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PATENT INFORMATION: US 2007105122 AI 20070510  
APPLICATION INFO.: US 2004-917503 AI 20040813 (10)  
RELATED APPLN. INFO.: Division of Ser. No. US 2000-629469, filed on 28 Jul  
2000, ABANDONED

NUMBER DATE

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PRIORITY INFORMATION: JP 1999-248036 19990929  
JP 1999-300253 19990827  
JP 2000-118776 20000111  
JP 2000-183767 20000502

JP 2000-241899 20000609  
US 1999-159590P 19991018 (60)  
US 2000-183322P 20000217 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: FOLEY AND LARDNER LLP, SUITE 500, 3000 K STREET NW,  
WASHINGTON, DC, 20007, US  
NUMBER OF CLAIMS: 23  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 3 Drawing Page(s)  
LINE COUNT: 96883

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Primers for synthesizing full-length cDNAs and their use are provided.  
5602 cDNA encoding a human protein has been isolated and nucleotide  
sequences of 5'-, and 3'-ends of the cDNA have been determined.  
Furthermore, primers for synthesizing the full-length cDNA have been  
provided to clarify the function of the protein encoded by the cDNA. The  
full-length cDNA of the present invention containing the translation  
start site provides information useful for analyzing the functions of  
the protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 3 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2007:12069 USPATFULL <<LOGINID::20080219>>

TITLE: Method for treating or inhibiting the effects of  
injuries or diseases that result in neuronal  
degeneration and method for promoting neurogenesis  
INVENTOR(S): Schwartz, Michal Eisenbach-, Rehovot, ISRAEL  
Lider, Ofer, Kfar Bilu Bet, ISRAEL  
Rolls, Asya, Rehovot, ISRAEL  
Cahalon, Liora, Givataim, ISRAEL  
Lider, Osnat, Kfar Bilu B., ISRAEL legal  
representative

PATENT ASSIGNEE(S): YEDA RESEARCH AND DEVELOPMENT CO. LTD., Rehovot, ISRAEL  
(non-U.S. corporation)

NUMBER KIND DATE

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PATENT INFORMATION: US 2007010484 A1 20070111  
APPLICATION INFO.: US 2006-473306 A1 20060623 (11)  
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2003-570989,  
PENDING A 371 of International Ser. No. WO  
2004-US29288, filed on 8 Sep 2004

NUMBER DATE

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PRIORITY INFORMATION: US 2003-500690P 20030908 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW,  
SUITE 300, WASHINGTON, DC, 20001-5303, US  
NUMBER OF CLAIMS: 28  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 11 Drawing Page(s)  
LINE COUNT: 2109

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Oligosaccharides, and in particular disaccharides, which are degradation  
products of chondroitin sulfate proteoglycan are effective for use in  
treating, inhibiting, or ameliorating the effects of injuries or  
diseases or disorders that result in or are caused by neuronal  
degeneration or of disorders resulting in mental and cognitive  
dysfunction. They are also useful for promoting neurogenesis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 16 IFIPAT COPYRIGHT 2008 IFI on STN

AN 11382395 IFIPAT;IFIUDB;IFICDB <<LOGINID::20080219>>  
TITLE: IDENTIFICATION OF NOVEL NOGO-RECEPTORS AND METHODS  
RELATED THERETO

INVENTOR(S): Giger, Roman J., Rochester, NY, US  
PATENT ASSIGNEE(S): Unassigned  
PATENT ASSIGNEE PROBABLE: Rochester, University of (Probable)  
AGENT: NEEDLE & ROSENBERG, P.C., SUITE 1000, 999 PEACHTREE  
STREET, ATLANTA, GA, 30309-3915, US

NUMBER	PK	DATE
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PATENT INFORMATION:	US 2007032406	A1 20070208
APPLICATION INFORMATION:	US 2004-551833	20040402
	WO 2004-US10328	20040402
	20060720	PCT 371 date
	20060720	PCT 102(e) date

NUMBER	DATE
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PRIORITY APPLN. INFO.:	US 2003-460849P 20030404 (Provisional)
FAMILY INFORMATION:	US 2007032406 20070208
DOCUMENT TYPE:	Utility
	Patent Application - First Publication
FILE SEGMENT:	CHEMICAL
	APPLICATION
ENTRY DATE:	Entered STN: 9 Feb 2007
	Last Updated on STN: 20 Mar 2007

PARENT CASE DATA:

This application claims the benefit of U.S. Provisional Application 60/460,849 filed Apr. 4, 2003, which is incorporated herein by reference in its entirety.

NUMBER OF CLAIMS: 64 20 Figure(s).

DESCRIPTION OF FIGURES:

FIG. 2 shows that Nogo receptors show broad but distinct \*\*\*expression\*\*\* in adulthood. Multi-tissue Northern blot analysis of adult rat, including brain (br), thymus (th), lung (lu), heart (ht), muscle (mu), stomach (st), small intestine (si), liver (lr), kidney (kd), spleen (sp), testis (ts), and skin (sk). FIG. 2(a) shows that NgR is a single transcript of 2.3-kb. FIG. 2(b) shows that NgR2 exists as a 2.3-kb (brain) and 2.0-kb (liver) transcript. FIG. 2(c) shows that NgR3 has a size of 3.8-kb, less abundant transcripts of 2.9-kb, and 2.0-kb are found as well. In liver and testis a 3.5-kb NgR3 transcript is found. FIG. 2(d) shows the actin control which ensures equal loading of RNA. FIG. 3 shows that nogo receptors show strikingly overlapping \*\*\*expression\*\*\* in the mature CNS. In all CNS structures examined, nogo receptors show strikingly similar \*\*\*expression\*\*\* patterns. Consecutive sections of different CNS regions were hybridized with probes specific for NgR (a,d,g,j,m,p), NgR2 (b,e,h,k,n,q), and NgR3 (c,f,i,l,o,r). In the retina (a-c), intense staining is localized to retinal ganglion cells and the inner nuclear layer (INL). Moderate \*\*\*expression\*\*\* is observed between the INL and the pigmented epithelium. In the neocortex (d-f), all three nogo receptors are strongly and broadly \*\*\*expressed\*\*\* in pyramidal cells. In the hippocampal formation (g-i), maximal staining is found in dentate granule cells, hilus, and CA3-CA1 pyramidal cells. In the cerebellum (j-l), granule cells and Purkinje cells are labeled. In the spinal cord (m-o), \*\*\*expression\*\*\* is confined to few cells in gray matter including motoneurons in the ventral horn. DRG (p-r), are heavily stained including large and small caliber neurons. FIG. 4 shows that Nogo receptors are glycoproteins enriched in lipid rafts isolated from postnatal brain and exist in soluble and membrane bound forms. NgR is enriched in lipid rafts (4a). NgR1 associated with lipid rafts has a molecular weight of 6570 kDa and exists in multiple isoelectric variants (4b). Caveolin, 22 kDa was used as a marker for lipid rafts and is shown as well (2-D gel). NgR1 can be stripped from brain membranes under high salt (0.5M NaCl) conditions (4c). The C-terminal part of NgR1 (residues 278-439) is glycosylated (4d). The C-terminal domain of NgR1 \*\*\*expressed\*\*\* in COS cells is approx 5 kDa larger than the corresponding construct \*\*\*expressed\*\*\* in E. coli (4d).

FIG. 5 shows that Nogo receptors show distinct binding preferences for the myelin inhibitors Nogo-66, MAG, and OMgp. FIG. 5(a) shows that \*\*\*recombinant\*\*\* NgRs are localized to the cell surface in COS-7. Anti-myc immunocytochemistry robustly labels NgR1 (a1), NgR2 (a2), and NgR3 (a3). Anti-NgR1 selectively reacts with NgR1 (a4), but not NgR2 and NgR3 (a5 and a6).

AntiNgR2 selectively recognizes NgR2 (a8), but not NgR1 and NgR3 (a7 and a9). FIG. 5(b) shows that the myelin-associated neurite outgrowth inhibitory molecules Nogo-66, MAG-Fc, and OMgp show overlapping but distinct binding to NgRs. In COS-7 cells ligand receptor interaction are as follows: Nogo-66 binds NgR1 (b1) but not NgR2 and NgR3 (b4 and b7); MAG-Fc binds NgR1 (b2), NgR2 (b5) but not NgR3 (b8); and OMgp binds NgR1 (b3) but not NgR2 (b6) and NgR3 (b9). The top panel of FIG. 5(c) is a summary of ligand binding to NgRs; the bottom panel of FIG. 5(c) shows Nogo-66 binding to chimeric NgRs, revealing multivalent and cooperative binding to the NgR1 LRR cluster. Adding or deleting LRR6 in NgR1 leads to a complete loss of binding.

FIG. 6 shows soluble NgRs (sNgRs) bind selectively to CNS white matter. Affinohistochemistry with soluble, AP-tagged sNgRs. FIGS. 6(A) and (B) show binding of sNgR1 to coronal brain section of E18 rat. High magnification of sNgR1 binding to E18 optic nerve (C), E20 cortical mantle (D), and P3 hippocampal formation (E). Robust staining of white matter is found, including all major fiber tracts. FIGS. 6(F-I) show a comparison of sNgR1 (F), sNgR2 (G), sNgR3 (H), and AP-only (I) to E18 coronal sections. Note, only sNgR1 and sNgR3 but not sNgR2 and AP-only bind to fiber tracts. FIGS. 6(J-M) binding of sNgR1 (J) and sNgR3 (K) to E18 spinal cord is identical, but clearly distinct from binding of Sema3A (L) and Sema3F (M). Binding to 1-week old spinal cord cross sections of sNgR1 (N), sNgR3 (O), Sema3A (P), and Sema3F (Q).

FIG. 7 shows NgRs are sialic acid binding lectins. Binding of sNgR1 and sNgR3 to brain is independent of p75NTR and major brain gangliosides. sNgR1 binding to neonate mouse brain tissue sections of (a1) wild-type, (a2) p75<sup>exonIII</sup> mutant, (a3) GlcNAc mutant, and (a4) GS3 synthase mutant mice. sNgR3 binding to neonate mouse brain tissue sections (a6) wild-type, (a7) p75<sup>exonIII</sup> mutant, (a8) GlcNAc mutant, and (a9) GS3 synthase mutant mice. Binding of sNgR1 but not NgR3 is sensitive to preincubation of ligand with polyclonal anti-NgR1C-term; (a5') sNgR1 preincubated with anti-NgR1C-term, (a5'') sNgR1 preincubated with preimmune serum, (a10') sNgR3 preincubated with anti-NgR1C-term, (a10'') sNgR3 preincubated with preimmune serum.

FIG. 7(b) shows Western blot analysis of AP-tagged fusion proteins of NgRs used for binding to brain tissue sections. Ligands were detected with anti-alkaline phosphatase antibody and had the predicted molecular weights. FIG. 7(c) depicts a schematic representation of sNgR1 deletion constructs used for binding to brain: intensity of binding to brain is indicated on the right: (+++, maximal binding), (++, moderate binding), (+, weak binding), (+-, marginal binding), (-no binding).

FIG. 7(d) details the alignment of presumptive sialic acid binding consensus sequences of NgR1, NgR2, NgR3, MAG (myelin associated \*\*\*glycoprotein\*\*\*), sn (sialoadhesin), L1, and TAG-1.

FIG. 7(e) shows that the binding of NgR1 and NgR3 is sensitive to pretreatment of brain tissue with sialidase (V. cholera neuraminidase=VCN). (e1') NgR1 bound to brain pretreated with enzyme buffer only, (e1'') NgR1 bound only weakly to brain pretreated with sialidase. (e2') NgR3 bound to brain pretreated with enzyme buffer only (e2'') NgR3 bound weakly to brain pretreated with sialidase. (e3') NgR2 bound not to brain pretreated with enzyme buffer only, (e3'') NgR2 bound not to brain pretreated with sialidase. (e4') Sema3F bound to brain pretreated with enzyme buffer only, (e4'') and Sema3F also bound to brain pretreated with sialidase.

FIG. 7(f) shows the quantification of binding of sNgR1 to brain tissue sections pretreated with N-acetylglucosaminidase (NAC), sialidase (Siase=V. cholera neuraminidase), \*\*\*Chondroitinase\*\*\* ABC (ABC), glycopeptidase F (GlyF) (sNgR1 binding is normalized to ligand binding observed to sections incubated with the corresponding enzyme buffer only).

FIG. 7(g) shows the quantification of binding of NgR3 to brain tissue sections pretreated with N-acetylglucosaminidase (NAC), sialidase (Siase), \*\*\*Chondroitinase\*\*\* ABC (ABC), glycopeptidase F (GlyF) (sNgR3 binding is normalized to ligand binding observed to sections incubated with the corresponding enzyme buffer only).

FIG. 8 shows that sNgR1 and sNgR3, but not sNgR2 bind GAGs. All binding is to E18 rat brain coronal sections: Removing the heparan sulfate binding motif (HSB) from the C-terminal end of sNgR1 completely abolishes binding to brain ((a1) AP-sNgR1CTu binds strongly to many fiber tracts, (a2) AP-sNgR1CTu Delta HS does not bind to brain). Similar to sNgR1, removing the HSB consensus binding motif of sNgR3 completely abolishes binding to brain ((a3) AP-sNgR3CTu binds strongly to many fiber tracts, (a4) AP-sNgR3CTu Delta HS does not bind to brain).

FIG. 9 shows the NgR1 C-terminal domain is necessary to signal myelin inhibition. Dissociated rat DRG neurons were cultured on cryosections of adult

human superior frontal gyrus (SFG). FIG. 9(a) shows E15 DRG neurons grow on gray matter (GM) and white matter (WM), the dotted line indicates the GM-WM border. FIG. 9(b) shows E15 DRG neurons show long fibers on poly-lysine, WM and GM. Postnatal day 5 (P5) DRG neurons show some growth on gray matter (c) and (d) but very little, if any growth on white matter (e). In the presence of anti-NgR1C-term antibody growth on gray matter (f) and white matter (g and h) is enhanced and comparable. Very little growth on both gray (i) and white matter (j) is observed in the presence of control IgG.

FIG. 10 shows a Scatchard plot analysis of the NgR2-MAG-Fc interaction. The dissociation constant of the interaction was determined to be 2 nM. (Small insert: saturation curve on NgR2 \*\*\*expressing\*\*\* COS-7 cells under increasing concentrations of MAG-Fc).

FIG. 11 shows adenoviral vector mediated \*\*\*expression\*\*\* of NgR2 (AdNgR2) in dissociated postnatal day 3 (P3) rat DRG cultures confers sialic acid dependent binding of MAG-Fc (b and e). Ectopic NgR1 (Ad-NgR1) in P3 DRG neurons supports MAG-Fc binding weakly (c) but strongly supports binding of AP-Nogo66 (Nogo66) (i). A control vector \*\*\*expressing\*\*\* red fluorescent protein (Ad-RFP) neither supports binding of MAG-Fc (a) nor Nogo66 (g.). Note, Nogo66 binding to NgR1 is not sensitive to neuraminidase treatment (i and l) (+sia=cultures pretreated with *V. cholerae* neuraminidase).

#### DESCRIPTION OF FIGURES:

FIG. 12(a) shows the structural basis of sialic acid dependence of the NgR2-MAG interaction. FIG. 12A-A" shows that wild-type NgR2 is expressed on the cell surface of transiently transfected COS-7 cells as shown by anti-NgR2 immunocytochemistry (ICC, see A"). NgR2 supports high affinity binding of MAG-Fc (MAG) but not AP-Nogo66 (Nogo66). FIG. 12BB" the NgR2-ligand binding domain (LBD=LRRNT+LRR+LRRCT=amino acid residues 1-314) is not sufficient to support high affinity MAG binding. FIGS. 12C-C"" shows the NgR2-'unique' domain (residues 315-420), when fused to the NgR1-LBD (residues 1-314) is sufficient to support high affinity MAG binding. FIG. 12DD" shows the NgR2-unique domain, when fused to the NgR3-LBD (residues 1-309) does not support MAG binding. FIG. 12E-E"" shows NgR2 sequences (residues 315-327) juxtaposed to the NgR2LBD are necessary for high affinity MAG binding. FIGS. 12FF"" shows that residues 1-353 of NgR1 fused to NgR2 residues 328-420 are not sufficient to support high affinity MAG binding. FIGS. 12G-G" shows that introducing a 13-amino acid NgR2peptide (Pro315-Ser327) juxtaposed to the NgR1-LBD is sufficient to convert NgR1 into a high affinity MAG binding receptor while maintaining the Nogo66 and OMgp binding capacity (called NgROMN). FIGS. 12H'-H" shows that mutating N325E in NgROMN greatly reduces MAG binding. FIG. 12(b) shows the alignment of the NgR1, NgR2, and NgR3 sequences juxtaposed to the LBDs, the SpeI restriction sites used to generate chimeric receptors are indicated. The 13 amino acid NgR2 peptide Pro315Ser327 is underlined. Amino acid N327 is labeled with an asterisk. FIG. 1c shows a quantification of the relative binding affinities of MAG to NgR chimeric receptors depicted in FIG. 12a. Binding is normalized to wild-type NgR2 (1) which is defined as 100%.

FIG. 13(A) shows Western blot analysis of different postnatal rat brain regions: Tissue homogenates of retina, cerebellum, neocortex (cortex), hippocampus, and entorhinal cortex were subjected to SDS-PAGE and probed with anti-NgR2, anti-NgR1, anti-p75NTR, or anti-actin antibody (as a loading control). NgR2 protein is more abundant in retina than in neocortex, hippocampus, and entorhinal cortex. Very low levels of NgR2 are found in the cerebellum. NgR1 on the other hand is most abundant in the neocortex and hippocampus, less expression is found in the entorhinal cortex and cerebellum and still less NgR1 protein is detected in the retina. P75NTR is most abundant in the retina, somewhat less in the cerebellum and is only weakly expressed in neocortex, hippocampus, and entorhinal cortex. Equal amounts of tissue homogenate were loaded in each lane as revealed by anti-actin staining. FIG.

13(B) shows that NgR2 binds NgR1: Co-immunoprecipitation experiment in HEK293T cells transfected with NgR1 only, NgR2 only, NgR1 and NgR2; or NgR1, NgR2, and p75NTR. Immunoprecipitation experiments were performed in the presence or absence of MAG-Fc (4  $\mu$ g/ml). For immunoprecipitation with anti-NgR1, IgG was coupled to BrCNactivated Sepharose (anti-NgR1beads). Independently of whether MAG-Fc was present, NgR1 and NgR2 interact with each other.

FIG. 14 shows NgR1 binds p75NTR: HEK293T cells were transfected with NgR1 only or NgR1 together with p75NTR. Immunoprecipitation with anti-NgR1 confirmed previous observations that NgR1 and p75NTR form an immune complex. The NgR1 heparan sulfate-binding (HSB) motif located toward its Cterminal end is not necessary for the interaction with p75NTR: a NgR1 deletion mutant lacking the HBS motif still associates with p75NTR. Co-expression of NgR2 and p75NTR

revealed that NgR2 associates with p75NTR, the association is ligand (MAG-Fc) independent.

FIG. 15 shows that NgR2 is a functional MAG receptor in postnatal neurons: In FIG. 15A postnatal day 7 (P7) rat cerebellar granule cells (CGCs) were transfected to either achieve ectopic expression of green fluorescence protein (GFP+) or NgR2 (NgR2+). Many CGCs are transfected (30-40%) as revealed by double staining with anti-GFP and the neuron specific marker anti-classIII tubulin (TuJ). Transfected CGCs were either cultured on control chinese hamster ovary cells (CHO-R2) or on CHO cells stably expressing MAG (CHO-MAG). FIG. 15B: immunoblotting of cultured P7 CGCs shows expression NgR1 and p75NTR but not NgR2. FIG. 15C: quantification of neurite length of cells described in panel 15A: ectopic expression of NgR2 in CGCs leads to a statistically significant ( $p < 0.001$ ) increase in MAG inhibition compared to CGCs ectopically expressing GFP. The numbers of neurons (n) counted under each condition is indicated in the FIG. 15C. Statistics program used (SigmaStat 3.0). FIG. 16 shows that fibroblast growth factor 2 (bFGF) is a high affinity ligand for NgR1 but not NgR2 or NgR3.!

AB Disclosed are compositions relating to the Nogo receptor (NgR) family as well as fragments, chimeras, and variants thereof. The invention provides polypeptides, nucleic acids, vectors, expression systems, and antibodies and antibody fragments related to the NgRs as well as uses thereof. Such uses include modulation neurite outgrowth in a subject and treatment of central nervous system disorders in a subject, as well as, methods of identifying and screening compounds that can be used for modulating neurite outgrowth in a subject or in treatment of central nervous system disorders in a subject.

CLMN 64 20 Figure(s).

FIG. 2 shows that Nogo receptors show broad but distinct

\*\*\*expression\*\*\* in adulthood. Multi-tissue Northern blot analysis of adult rat, including brain (br), thymus (th), lung (lu), heart (ht), muscle (mu), stomach (st), small intestine (si), liver (lr), kidney (kd), spleen (sp), testis (ts), and skin (sk). FIG. 2(a) shows that NgR is a single transcript of 2.3-kb. FIG. 2(b) shows that NgR2 exists as a 2.3-kb (brain) and 2.0-kb (liver) transcript. FIG. 2(c) shows that NgR3 has a size of 3.8-kb, less abundant transcripts of 2.9-kb, and 2.0-kb are found as well. In liver and testis a 3.5-kb NgR3 transcript is found. FIG. 2(d) shows the actin control which ensures equal loading of RNA.

FIG. 3 shows that nogo receptors show strikingly overlapping

\*\*\*expression\*\*\* in the mature CNS. In all CNS structures examined, nogo receptors show strikingly similar \*\*\*expression\*\*\* patterns. Consecutive sections of different CNS regions were hybridized with probes specific for NgR (a,d,g,j,m,p), NgR2 (b,e,h,k,n,q), and NgR3 (c,f,i,l,o,r). In the retina (a-c), intense staining is localized to retinal ganglion cells and the inner nuclear layer (INL). Moderate

\*\*\*expression\*\*\* is observed between the INL and the pigmented epithelium. In the neocortex (d-f), all three nogo receptors are strongly and broadly \*\*\*expressed\*\*\* in pyramidal cells. In the hippocampal formation (g-i), maximal staining is found in dentate granule cells, hilus, and CA3-CA1 pyramidal cells. In the cerebellum (j-l), granule cells and Purkinje cells are labeled. In the spinal cord (m-o),

\*\*\*expression\*\*\* is confined to few cells in gray matter including motoneurons in the ventral horn. DRG (p-r), are heavily stained including large and small caliber neurons.

FIG. 4 shows that Nogo receptors are glycoproteins enriched in lipid rafts isolated from postnatal brain and exist in soluble and membrane bound forms. NgR is enriched in lipid rafts (4a). NgR1 associated with lipid rafts has a molecular weight of 6570 kDa and exists in multiple isoelectric variants (4b). Caveolin, 22 kDa was used as a marker for lipid rafts and is shown as well (2-D gel). NgR1 can be stripped from brain membranes under high salt (0.5M NaCl) conditions (4c). The C-terminal part of NgR1 (residues 278-439) is glycosylated (4d). The C-terminal domain of NgR1 \*\*\*expressed\*\*\* in COS cells is approx 5 kDa larger than the corresponding construct \*\*\*expressed\*\*\* in E. coli (4d).

FIG. 5 shows that Nogo receptors show distinct binding preferences for the myelin inhibitors Nogo-66, MAG, and OMgp. FIG. 5(a) shows that

\*\*\*recombinant\*\*\* NgRs are localized to the cell surface in COS-7. Anti-myc immunocytochemistry robustly labels NgR1 (a1), NgR2 (a2), and NgR3 (a3). Anti-NgR1 selectively reacts with NgR1 (a4), but not NgR2 and NgR3 (a5 and a6). AntiNgR2 selectively recognizes NgR2 (a8), but not NgR1

and NgR3 (a7 and a9). FIG. 5(b) shows that the myelin-associated neurite outgrowth inhibitory molecules Nogo-66, MAG-Fc, and OMgp show overlapping but distinct binding to NgRs. In COS-7 cells ligand receptor interaction are as follows: Nogo-66 binds NgR1 (b1) but not NgR2 and NgR3 (b4 and b7); MAG-Fc binds NgR1 (b2), NgR2 (b5) but not NgR3 (b8); and OMgp binds NgR1 (b3) but not NgR2 (b6) and NgR3 (b9). The top panel of FIG. 5(c) is a summary of ligand binding to NgRs; the bottom panel of FIG. 5(c) shows Nogo-66 binding to chimeric NgRs, revealing multivalent and cooperative binding to the NgR1 LRR cluster. Adding or deleting LRR6 in NgR1 leads to a complete loss of binding.

FIG. 6 shows soluble NgRs (sNgRs) bind selectively to CNS white matter. Affinohistochemistry with soluble, AP-tagged sNgRs. FIGS. 6(A) and (B) show binding of sNgR1 to coronal brain section of E18 rat. High magnification of sNgR1 binding to E18 optic nerve (C), E20 cortical mantle (D), and P3 hippocampal formation (E). Robust staining of white matter is found, including all major fiber tracts. FIGS. 6(F-I) show a comparison of sNgR1 (F), sNgR2 (G), sNgR3 (H), and AP-only (I) to E18 coronal sections. Note, only sNgR1 and sNgR3 but not sNgR2 and AP-only bind to fiber tracts. FIGS. 6(J-M) binding of sNgR1 (J) and sNgR3 (K) to E18 spinal cord is identical, but clearly distinct from binding of Sema3A (L) and Sema3F (M). Binding to 1-week old spinal cord cross sections of sNgR1 (N), sNgR3 (O), Sema3A (P), and Sema3F (Q).

FIG. 7 shows NgRs are sialic acid binding lectins. Binding of sNgR1 and sNgR3 to brain is independent of p75NTR and major brain gangliosides. sNgR1 binding to neonate mouse brain tissue sections of (a1) wild-type, (a2) p75<sup>exonIII</sup> mutant, (a3) GlcNAc mutant, and (a4) GS3 synthase mutant mice. sNgR3 binding to neonate mouse brain tissue sections (a6) wild-type, (a7) p75<sup>exonIII</sup> mutant, (a8) GlcNAc mutant, and (a9) GS3 synthase mutant mice. Binding of sNgR1 but not NgR3 is sensitive to preincubation of ligand with polyclonal anti-NgR1C-term; (a5') sNgR1 preincubated with anti-NgR1C-term, (a5'') sNgR1 preincubated with preimmune serum, (a10') sNgR3 preincubated with anti-NgR1C-term, (a10'') sNgR3 preincubated with preimmune serum.

FIG. 7(b) shows Western blot analysis of AP-tagged fusion proteins of NgRs used for binding to brain tissue sections. Ligands were detected with anti-alkaline phosphatase antibody and had the predicted molecular weights. FIG. 7(c) depicts a schematic representation of sNgR1 deletion constructs used for binding to brain: intensity of binding to brain is indicated on the right: (+++, maximal binding), (++, moderate binding), (+, weak binding), (+-, marginal binding), (-no binding).

FIG. 7(d) details the alignment of presumptive sialic acid binding consensus sequences of NgR1, NgR2, NgR3, MAG (myelin associated \*\*\*glycoprotein\*\*\*), sn (sialoadhesin), L1, and TAG-1.

FIG. 7(e) shows that the binding of NgR1 and NgR3 is sensitive to pretreatment of brain tissue with sialidase (V. cholera neuraminidase=VCN). (e1') NgR1 bound to brain pretreated with enzyme buffer only, (e1'') NgR1 bound only weakly to brain pretreated with sialidase. (e2') NgR3 bound to brain pretreated with enzyme buffer only (e2'') NgR3 bound weakly to brain pretreated with sialidase. (e3') NgR2 bound not to brain pretreated with enzyme buffer only, (e3'') NgR2 bound not to brain pretreated with sialidase. (e4') Sema3F bound to brain pretreated with enzyme buffer only, (e4'') and Sema3F also bound to brain pretreated with sialidase.

FIG. 7(f) shows the quantification of binding of sNgR1 to brain tissue sections pretreated with N-acetylglucosaminidase (NAC), sialidase (Siase=V. cholera neuraminidase), \*\*\*Chondroitinase\*\*\* ABC (ABC), glycopeptidase F (GlyF) (sNgR1 binding is normalized to ligand binding observed to sections incubated with the corresponding enzyme buffer only).

FIG. 7(g) shows the quantification of binding of NgR3 to brain tissue sections pretreated with N-acetylglucosaminidase (NAC), sialidase (Siase), \*\*\*Chondroitinase\*\*\* ABC (ABC), glycopeptidase F (GlyF) (sNgR3 binding is normalized to ligand binding observed to sections incubated with the corresponding enzyme buffer only).

FIG. 8 shows that sNgR1 and sNgR3, but not sNgR2 bind GAGs. All binding is to E18 rat brain coronal sections: Removing the heparan sulfate binding motif (HSB) from the C-terminal end of sNgR1 completely abolishes binding to brain ((a1) AP-sNgR1CTu binds strongly to many fiber tracts, (a2) AP-sNgR1CTu Delta HS does not bind to brain). Similar to sNgR1, removing the HSB consensus binding motif of sNgR3 completely abolishes binding to

brain ((a3) AP-sNgR3CTu binds strongly to many fiber tracts, (a4) AP-sNgR3CTu Delta HS does not bind to brain).

FIG. 9 shows the NgR1 C-terminal domain is necessary to signal myelin inhibition. Dissociated rat DRG neurons were cultured on cryosections of adult human superior frontal gyrus (SFG). FIG. 9(a) shows E15 DRG neurons grow on gray matter (GM) and white matter (WM), the dotted line indicates the GM-WM border. FIG. 9(b) shows E15 DRG neurons show long fibers on poly-lysine, WM and GM. Postnatal day 5 (P5) DRG neurons show some growth on gray matter (c) and (d) but very little, if any growth on white matter (e). In the presence of anti-NgR1C-term antibody growth on gray matter (f) and white matter (g and h) is enhanced and comparable. Very little growth on both gray (i) and white matter (j) is observed in the presence of control IgG.

FIG. 10 shows a Scatchard plot analysis of the NgR2-MAG-Fc interaction. The dissociation constant of the interaction was determined to be 2 nM. (Small insert: saturation curve on NgR2 \*\*\*expressing\*\*\* COS-7 cells under increasing concentrations of MAG-Fc).

FIG. 11 shows adenoviral vector mediated \*\*\*expression\*\*\* of NgR2 (AdNgR2) in dissociated postnatal day 3 (P3) rat DRG cultures confers sialic acid dependent binding of MAG-Fc (b and e). Ectopic NgR1 (Ad-NgR1) in P3 DRG neurons supports MAG-Fc binding weakly (c) but strongly supports binding of AP-Nogo66 (Nogo66) (i). A control vector \*\*\*expressing\*\*\* red fluorescent protein (Ad-RFP) neither supports binding of MAG-Fc (a) nor Nogo66 (g.). Note, Nogo66 binding to NgR1 is not sensitive to neuraminidase treatment (i and l) (+sia=cultures pretreated with V. cholerae neuraminidase).

FIG. 12(a) shows the structural basis of sialic acid dependence of the NgR2-MAG interaction. FIG. 12A-A" shows that wild-type NgR2 is expressed on the cell surface of transiently transfected COS-7 cells as shown by anti-NgR2 immunocytochemistry (ICC, see A"). NgR2 supports high affinity binding of MAG-Fc (MAG) but not AP-Nogo66 (Nogo66). FIG. 12BB" the NgR2-ligand binding domain (LBD=LRRNT+LRR+LRRCT=amino acid residues 1-314) is not sufficient to support high affinity MAG binding. FIGS. 12C-C"" shows the NgR2-'unique' domain (residues 315-420), when fused to the NgR1-LBD (residues 1-314) is sufficient to support high affinity MAG binding. FIG. 12DD" shows the NgR2-unique domain, when fused to the NgR3-LBD (residues 1-309) does not support MAG binding. FIG. 12E-E"" shows NgR2 sequences (residues 315-327) juxtaposed to the NgR2LBD are necessary for high affinity MAG binding. FIGS. 12FF"" shows that residues 1-353 of NgR1 fused to NgR2 residues 328-420 are not sufficient to support high affinity MAG binding. FIGS. 12G-G" shows that introducing a 13-amino acid NgR2peptide (Pro315-Ser327) juxtaposed to the NgR1-LBD is sufficient to convert NgR1 into a high affinity MAG binding receptor while maintaining the Nogo66 and OMgp binding capacity (called NgROMN). FIGS. 12H'-H" shows that mutating N325E in NgROMN greatly reduces MAG binding. FIG. 12(b) shows the alignment of the NgR1, NgR2, and NgR3 sequences juxtaposed to the LBDs, the SpeI restriction sites used to generate chimeric receptors are indicated. The 13 amino acid NgR2 peptide Pro315Ser327 is underlined. Amino acid N327 is labeled with an asterisk. FIG. 1c shows a quantification of the relative binding affinities of MAG to NgR chimeric receptors depicted in FIG. 12a. Binding is normalized to wild-type NgR2 (1) which is defined as 100%.

FIG. 13(A) shows Western blot analysis of different postnatal rat brain regions: Tissue homogenates of retina, cerebellum, neocortex (cortex), hippocampus, and entorhinal cortex were subjected to SDS-PAGE and probed with anti-NgR2, anti-NgR1, anti-p75NTR, or anti-actin antibody (as a loading control). NgR2 protein is more abundant in retina than in neocortex, hippocampus, and entorhinal cortex. Very low levels of NgR2 are found in the cerebellum. NgR1 on the other hand is most abundant in the neocortex and hippocampus, less expression is found in the entorhinal cortex and cerebellum and still less NgR1 protein is detected in the retina. P75NTR is most abundant in the retina, somewhat less in the cerebellum and is only weakly expressed in neocortex, hippocampus, and entorhinal cortex. Equal amounts of tissue homogenate were loaded in each lane as revealed by anti-actin staining. FIG. 13(B) shows that NgR2 binds NgR1: Co-immunoprecipitation experiment in HEK293T cells transfected with NgR1 only, NgR2 only, NgR1 and NgR2; or NgR1, NgR2, and p75NTR. Immunoprecipitation experiments were performed in the presence or absence of MAG-Fc (4  $\mu$ g/ml). For immunoprecipitation with anti-NgR1, IgG was coupled to BrCNactivated Sepharose (anti-NgR1beads). Independently of



whether MAG-Fc was present, NgR1 and NgR2 interact with each other. FIG. 14 shows NgR1 binds p75NTR: HEK293T cells were transfected with NgR1 only or NgR1 together with p75NTR. Immunoprecipitation with anti-NgR1 confirmed previous observations that NgR1 and p75NTR form an immune complex. The NgR1 heparan sulfate-binding (HSB) motif located toward its Cterminal end is not necessary for the interaction with p75NTR: a NgR1 deletion mutant lacking the HBS motif still associates with p75NTR. Co-expression of NgR2 and p75NTR revealed that NgR2 associates with p75NTR, the association is ligand (MAG-Fc) independent. FIG. 15 shows that NgR2 is a functional MAG receptor in postnatal neurons: In FIG. 15A postnatal day 7 (P7) rat cerebellar granule cells (CGCs) were transfected to either achieve ectopic expression of green fluorescence protein (GFP+) or NgR2 (NgR2+). Many CGCs are transfected (30-40%) as revealed by double staining with anti-GFP and the neuron specific marker anti-classIII tubulin (TuJ). Transfected CGCs were either cultured on control chinese hamster ovary cells (CHO-R2) or on CHO cells stably expressing MAG (CHO-MAG). FIG. 15B: immunoblotting of cultured P7 CGCs shows expression NgR1 and p75NTR but not NgR2. FIG. 15C: quantification of neurite length of cells described in panel 15A: ectopic expression of NgR2 in CGCs leads to a statistically significant ( $p < 0.001$ ) increase in MAG inhibition compared to CGCs ectopically expressing GFP. The numbers of neurons (n) counted under each condition is indicated in the FIG. 15C. Statistics program used (SigmaStat 3.0). FIG. 16 shows that fibroblast growth factor 2 (bFGF) is a high affinity ligand for NgR1 but not NgR2 or NgR3.!

L7 ANSWER 5 OF 16 USPATFULL on STN  
 ACCESSION NUMBER: 2006:111712 USPATFULL <<LOGINID::20080219>>  
 TITLE: Antagonist peptides to the C5A chemotactic function of  
 vitamin D binding protein  
 INVENTOR(S): Kew, Richard R., Miller Place, NY, UNITED STATES  
 Zhang, Jianhua, Stony Brook, NY, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2006094659 A1 20060504  
 APPLICATION INFO.: US 2005-243960 A1 20051005 (11)

NUMBER DATE

PRIORITY INFORMATION: US 2004-616105P 20041005 (60)  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: APPLICATION  
 LEGAL REPRESENTATIVE: SCULLY SCOTT MURPHY & PRESSER, PC, 400 GARDEN CITY  
 PLAZA, SUITE 300, GARDEN CITY, NY, 11530, US  
 NUMBER OF CLAIMS: 17  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 15 Drawing Page(s)  
 LINE COUNT: 2001  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB It has been demonstrated that one of Vitamin D Binding Protein (DBP)  
 biological functions is to enhance the chemotactic activity of C5a and  
 C5a des Arg. The present invention has found that peptides having  
 sequences that substantially correspond to a specific region in the  
 N-terminal domain I of DBP can block the DBP enhancement of C5a or C5a  
 des Arg chemotactic activity. Based in this discovery the present  
 invention provides DBP antagonist peptides and the use thereof for the  
 treatment C5a or C5a des Arg-mediated disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 16 USPATFULL on STN  
 ACCESSION NUMBER: 2005:176915 USPATFULL <<LOGINID::20080219>>  
 TITLE: Methods and compositions for promoting axon  
 regeneration and cell replacement therapy  
 INVENTOR(S): Chen, Dong Feng, Newton, MA, UNITED STATES  
 Cho, Kin-Sang, Winchester, MA, UNITED STATES  
 Takeda, Masumi, Boston, MA, UNITED STATES  
 Kinouchi, Reiko, Hokkaido, JAPAN

NUMBER KIND DATE

PATENT INFORMATION: US 2005152995 A1 20050714  
APPLICATION INFO.: US 2004-877066 A1 20040625 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2003-483528P 20030627 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: FOLEY HOAG, LLP, PATENT GROUP, WORLD TRADE CENTER WEST,  
155 SEAPORT BLVD, BOSTON, MA, 02110, US  
NUMBER OF CLAIMS: 47  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 17 Drawing Page(s)  
LINE COUNT: 3374  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided herein are methods and compositions for rendering a cellular environment permissive to axon regeneration and neural cell transplantation. Methods for stimulating axon regeneration in adult subjects are also disclosed. The methods may comprise contacting a tissue with an agent that prevents glial scar formation, such as by inhibiting reactive astroglial cells, and optionally an agent that increases bcl-2 protein levels in neural cells. Exemplary agents include astrotoxin for inhibiting reactive astroglial cells and lithium for increasing bcl-2 protein levels.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 16 WPIDS COPYRIGHT 2008 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2004-525770 [50] WPIDS  
DOC. NO. CPI: C2004-193443 [50]  
TITLE: New purified chondroitinase glycoprotein (CHASEGP)  
comprising a CHASEGP polypeptide and a N-linked sugar moiety, useful in preparing a composition for treating or preventing scarring  
DERWENT CLASS: B04; C06; D16  
INVENTOR: BOOKBINDER L H; FROST G I; KUNDU A; BOOKBINDER L; FROST G  
PATENT ASSIGNEE: (DELI-N) DELIATROPH PHARM INC; (HALO-N) HALOZYME INC  
COUNTRY COUNT: 103

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004058147	A2	20040715	(200450)*	EN	106[0]	
AU 2003297199	A1	20040722	(200476)	EN		
EP 1636248	A2	20060322	(200621)	EN		
AU 2003297199	A8	20051117	(200638)	EN		
US 20070148156	A1	20070628	(200743)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004058147	A2	WO 2003-US40090	20031215
AU 2003297199	A1	AU 2003-297199	20031215
AU 2003297199	A8	AU 2003-297199	20031215
EP 1636248	A2	EP 2003-814054	20031215
EP 1636248	A2	WO 2003-US40090	20031215
US 20070148156	A1 Provisional	US 2002-433532P	20021216
US 20070148156	A1	WO 2003-US40090	20031215
US 20070148156	A1	US 2006-539110	20060419

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003297199	A1 Based on	WO 2004058147 A
EP 1636248	A2 Based on	WO 2004058147 A

PRIORITY APPLN. INFO: US 2002-433532P 20021216

US 2006-539110 20060419

AN 2004-525770 [50] WPIDS

AB WO 2004058147 A2 UPAB: 20050530

NOVELTY - A new substantially purified chondroitinase glycoprotein (CHASEGP) comprises a CHASEGP polypeptide and at least 1 N-linked sugar moiety that is covalently attached to an asparagine residue of the polypeptide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a nucleic acid molecule comprising a sequence of nucleotides that encodes the polypeptide;
- (2) a vector comprising the nucleic acid molecule;
- (3) a cell comprising the vector;
- (4) a recombinant non-human animal, where an endogenous gene that encodes the polypeptide has been deleted or inactivated by homologous recombination or insertional mutagenesis of the animal or its ancestor;
- (5) a method for generating soluble recombinant CHASEGP;
- (6) a method for generating the CHASEGP;
- (7) a composition comprising the substantially purified CHASEGP glycoprotein in conjunction with a carrier; and
- (8) a method for treating an animal suffering from an excess of CHASEGP substrate.

ACTIVITY - Vulnerary.

No biological data given.

MECHANISM OF ACTION - Cell therapy.

USE - The chondroitinase glycoprotein (CHASEGP) is useful in preparing a composition for treating an animal suffering from an excess of CHASEGP substrate (claimed) for treating or preventing scarring.

L7 ANSWER 8 OF 16 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on  
STN DUPLICATE

ACCESSION NUMBER: 2002235003 ESBIOBASE <<LOGINID::20080219>>

TITLE: Molecular cloning and characterization of a novel  
chondroitin sulfate glucuronyltransferase that  
transfers glucuronic acid to N-acetylgalactosamine

AUTHOR: Gotoh M.; Yada T.; Sato T.; Akashima T.; Iwasaki H.;  
Mochizuki H.; Inaba N.; Togayachi A.; Kudo T.;  
Watanabe H.; Kimata K.; Narimatsu H.

CORPORATE SOURCE: H. Narimatsu, Research Center for Glycoscience, Natl.  
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SOURCE: Journal of Biological Chemistry, (11 OCT 2002), 277/41  
(38179-38188), 48 reference(s)  
CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We found a novel human \*\*\*gene\*\*\* (GenBank.TM. accession number AB037823, Kazusa DNA Research Institute KIAA1402) that possesses homology with chondroitin synthase. The full-length open reading frame consists of 772 amino acids and encodes a typical type II membrane protein. This enzyme had a domain containing .beta.3- \*\*\*glycosyltransferase\*\*\* motifs, which might be a .beta.3-glucuronyltransferase domain, but no domain with .beta.4- \*\*\*glycosyltransferase\*\*\* motifs, although both are found in chondroitin synthase. The putative catalytic domain was \*\*\*expressed\*\*\* in COS-7 cells as a soluble enzyme. Its glucuronyltransferase activity was observed when chondroitin and chondroitin sulfate polysaccharides and oligosaccharides were used as acceptor substrates. However, it was not detected when dermatan sulfate, hyaluronan, heparan sulfate, heparin, N-acetylheparosan, lactosamine tetrasaccharide, and linkage tri- and tetrasaccharide acceptors were employed. The reaction product, which was speculated to exhibit a GlcA.beta.1-3GalNAc linkage structure at its non-reducing terminus, showed the following characteristics. 1) It was catabolized by .beta.-glucuronidase. 2) It was an acceptor for Escherichia coli K4

chondroitin polymerase (K4 chondroitin polymerase). 3) The product of K4 chondroitin polymerase was cleaved by \*\*\*chondroitinase\*\*\* ACII. On the other hand, no N-acetylgalactosaminyltransferase activity was detected toward any acceptors. Quantitative real time PCR analysis revealed that its transcripts were highly \*\*\*expressed\*\*\* in the placenta, small intestine, and pancreas, although they were ubiquitously \*\*\*expressed\*\*\* in various tissues and cell lines. This enzyme could play a role in the synthesis of chondroitin sulfate as a glucuronyltransferase.

L7 ANSWER 9 OF 16 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE

ACCESSION NUMBER: 2001102424 ESBIOBASE <<LOGINID::20080219>>

TITLE: Production of prostaglandin D synthase as a keratan sulfate proteoglycan by cultured bovine keratocytes

AUTHOR: Berryhill B.L.; Beales M.P.; Hassell J.R.

CORPORATE SOURCE: B.L. Berryhill, CRS DPO, Shriners Hospital for Children, 12502 North Pine Drive, Tampa, FL 33612-9499, United States.

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SOURCE: Investigative Ophthalmology and Visual Science, (2001), 42/6 (1201-1207), 38 reference(s)  
CODEN: IOVSDA ISSN: 0146-0404

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Purpose. To characterize the major proteoglycans produced and secreted by collagenase-isolated bovine keratocytes in culture. Methods. Freshly isolated keratocytes from mature bovine corneas were cultured in serum-free Dulbecco's modified Eagle's medium/F12. Secreted proteoglycans were radiolabeled with protein labeling mix (.sup.3.sup.5S-

\*\*\*Express\*\*\*; Dupont NEN Life Science Products, Boston, MA) and digested with \*\*\*chondroitinase\*\*\* ABC, keratanase, and endo-.beta.-galactosidase to remove glycosaminoglycan chains, and core proteins were analyzed by autoradiography and Western blot analysis. An unidentified keratan sulfate proteoglycan (KSPG) was purified by gel filtration (Superose 6; Amersham Pharmacia, Piscataway, NJ) and anion-exchange chromatography (Resource Q; Amersham Pharmacia) and subjected to amino acid sequencing. Results. Keratanase digestion of proteoglycans produced .apprx.50 kDa core proteins that immunoreacted with antisera to lumican, keratocan, and osteoglycin-mimican.

\*\*\*Chondroitinase\*\*\* ABC digestion produced a .apprx.55-kDa core protein that immunoreacted with antisera to decorin. A 28-kDa band generated by keratanase or endo-.beta.-galactosidase digestion did not react with these antibodies. Chromatographic purification and amino acid sequencing revealed that the protein was prostaglandin D synthase (PGDS). Identity was confirmed by Western blot analysis using antisera to

\*\*\*recombinant\*\*\* PGDS. PGDS isolated from corneal extracts was not keratanase sensitive but was susceptible to endo-.beta.-galactosidase, suggesting that it contains unsulfated polylactosamine chains in native tissue and is therefore present as a \*\*\*glycoprotein\*\*\*. Conclusions. These results indicate that bovine keratocytes, when cultured under serum-free conditions, produce the four known leucine-rich proteoglycans decorin, keratocan, lumican, and osteoglycin/mimican and maintain a phenotype that is comparable to that of in situ keratocytes. Additionally, these cells produce PGDS, a known retinoid transporter, as a KSPG.

L7 ANSWER 10 OF 16 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V. on STN DUPLICATE

ACCESSION NUMBER: 1998094893 ESBIOBASE <<LOGINID::20080219>>

TITLE: The glycosylation sites and structural characteristics of oligosaccharides on recombinant human thrombomodulin

AUTHOR: Edano T.; Kumai N.; Mizoguchi T.; Ohkuchi M.

CORPORATE SOURCE: T. Edano, Tokyo Research Laboratories, Kowa Co. Ltd., Noguchi-oho, Higashimurayama, Tokyo 189, Japan.

SOURCE: International Journal of Biochemistry and Cell Biology, (1998), 30/1 (77-88), 24 reference(s)

CODEN: IJBBFU ISSN: 1357-2725  
PUBLISHER ITEM IDENT.: S1357272597000782  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United Kingdom  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Thrombomodulin (TM) is an anticoagulant \*\*\*glycoprotein\*\*\* on the surface of endothelial cell that directly inhibits the procoagulant activities of thrombin, and the TM-thrombin complex accelerates thrombin-catalyzed activation of protein C. Soluble TM in urine has no glycosaminoglycan (GAG) chain which accelerates the anticoagulant activities. Therefore, we \*\*\*expressed\*\*\* \*\*\*recombinant\*\*\* GAG-modified urinary thrombomodulin (GAG-UTM) in C127 cells. The glycosylation sites were determined by amino acid \*\*\*sequence\*\*\* analysis of peptides digested with trypsin after S-carboxymethylation. The structures of N-linked oligosaccharides were estimated by two-dimensional sugar mapping of pyridylaminated oligosaccharides that were treated with exoglycosidase. The disaccharide composition analysis of the GAG chain was performed by HPLC using digestion with \*\*\*chondroitinase\*\*\* ABC, ACII and B. Consequently, it was revealed that the N-linked oligosaccharides were assigned to Asn29, Ash98, Asn364, Asn391; those structures were estimated biantennary, 2-6 branched triantennary and 2-4 branched triantennary complex type oligosaccharides that were linked by fucose at the ratio of 1.0:0.5:0.1, respectively. Moreover, the attachment site of the GAG chain was assigned to Ser472. It was then estimated that the GAG chain contained chondroitin-4-sulfate and dermatan sulfate, which were repeated approximately 30 times. In this paper, the GAG attachment site and structural characteristics of GAG-UTM, were confirmed. Moreover, structures of the N-linked oligosaccharides of GAG-UTM are described for the first time.

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ACCESSION NUMBER: 1997:520603 SCISEARCH <<LOGINID::20080219>>  
THE GENUINE ARTICLE: XJ478

TITLE: Immortalized gastric epithelial cell line GSM06  
synthesizes hyaluronan under the influence of simian virus  
40 large T-antigen expression

AUTHOR: Goso Y (Reprint); Nakano S; Sugiyama N; Tabuchi Y;  
Horiuchi T; Hotta K

CORPORATE SOURCE: KITASATO UNIV, SCH MED, DEPT BIOCHEM, 1-15-1 KITASATO,  
SAGAMIHARA, KANAGAWA 228, JAPAN (Reprint); KITASATO UNIV,  
SCH MED, DEPT INTERNAL MED, SAGAMIHARA, KANAGAWA 228,  
JAPAN; DAIICHI PHARMACEUT CO LTD, BASIC TECHNOL RES LAB,  
EDOGAWA KU, TOKYO 134, JAPAN; DAIICHI PHARMACEUT CO LTD,  
NEW PROD RES LABS 3, EDOGAWA KU, TOKYO 134, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: JOURNAL OF BIOCHEMISTRY, (JUL 1997) Vol. 122, No. 1, pp.  
96-100.

ISSN: 0021-924X.

PUBLISHER: JAPANESE BIOCHEMICAL SOC, ISHIKAWA BLDG-3F, 25-16  
HONGO-5-CHOME, BUNKYO-KU, TOKYO 113, JAPAN.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 20

ENTRY DATE: Entered STN: 1997

Last Updated on STN: 1997

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB GSM06 is a cell line established from the stomach of transgenic mouse harboring a temperature-sensitive simian virus 40 (SV40) large T-antigen \*\*\*gene\*\*\*, H-3-labeled macromolecules produced by the cells incubated with [H-3] glucosamine were characterized to examine whether or not GSM06 cells synthesize mucin (mucus \*\*\*glycoprotein\*\*\*), The GSM06 cells grew until a confluent monolayer formed at 33 degrees C (the permissive temperature for SV40 large T-antigen \*\*\*expression\*\*\*), and the H-3-labeled macromolecules appeared in both cell extract and medium during culture for at least 1 week. Unexpectedly, almost all H-3-labeled macromolecules, which were excluded from a column of Sepharose CL-4B, were identified as hyaluronan by analyses using Sepharose CL-BB chromatography,

cesium trifluoroacetate equilibrium centrifugation, treatment with dithiothreitol, and trypsin, hyaluronidase, and \*\*\*chondroitinase\*\*\* ABC digestion. At a nonpermissive temperature (39 degrees C), GSM06 cells grew only slightly, but produced much more hyaluronan than at 33 degrees C. The results indicate that GSM06 cells produce not mucin, but hyaluronan, and that the expression of large T-antigen may influence hyaluronan synthesis in GSM06 cells.

L7 ANSWER 12 OF 16 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.  
on STN DUPLICATE

ACCESSION NUMBER: 1996068555 ESBIOBASE <<LOGINID::20080219>>

TITLE: Bovine herpesvirus 1 U(S) open reading frame 4 encodes  
a glycoproteoglycan

AUTHOR: Keil G.M.; Engelhardt T.; Karger A.; Enz M.

CORPORATE SOURCE: G.M. Keil, Inst. for Molec./Cellular Virology, FRCVDA,  
Friedrich-Loeffler-Institutes, D-17498 Insel Riems,  
Germany.

SOURCE: Journal of Virology, (1996), 70/5 (3032-3038)

CODEN: JOVIAM ISSN: 0022-538X

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB \*\*\*Sequence\*\*\* analysis of the short unique (U(S)) segment of the bovine herpesvirus 1 (BHV-1) genome predicted that the U(S) open reading frame (ORF) 4 encodes a protein with homology to \*\*\*glycoprotein\*\*\* G (gG) of other alpha- herpesviruses (P. Leung-Tack, J.-C. Audonnet, and M. Riviere, Virology 199:409-421, 1994). RNA analysis showed that the U(S) ORF4 is contained within two transcripts of 3.5 and 1.8 kb. The 3.5 kb RNA represents a structurally bicistronic RNA which encompasses the U(S) ORF3 and U(S) ORF4, whereas the 1.8-kb RNA constitutes the monocistronic U(S) ORF4 mRNA. To identify the predicted BHV-1 gG, \*\*\*recombinant\*\*\* vaccinia virus \*\*\*expressing\*\*\* the U(S) ORF4 was used to raise specific antibodies in rabbits. The antiserum recognized a 65-kDa polypeptide and a very diffusely migrating species of proteins with an apparent molecular mass of between 90 and greater than 240 kDa in supernatants of BHV-1-infected cells which was also precipitated together with 61- and 70-kDa polypeptides from cell-associated proteins. The specificity of the reaction was demonstrated by the absence of these proteins from the supernatant of cells infected with the U(S) ORF4 deletion mutant BHV-1/gp1-8. Treatment of the immunoprecipitated proteins with glycosidases and \*\*\*chondroitinase\*\*\* AC showed that the 65-kDa protein constitutes gG, which contains both N- and O-linked carbohydrates, and that the high-molecular- mass proteins contain glycosaminoglycans linked to a 65-kDa \*\*\*glycoprotein\*\*\* that is antigenically related to gG. These molecules were therefore named glycoproteoglycan G (gpgG). Pulse chase experiments indicated that gG and gpgG were processed from a common precursor molecule with an apparent molecular mass of 61 kDa via a 70-kDa intermediate. Both gG and gpgG could not be found associated with purified virions. In summary, our results identify the BHV-1 gG protein and demonstrate the presence of a form of posttranslational modification, glycosamino-glycosylation, that has not yet been described for a herpesvirus-encoded protein.

L7 ANSWER 13 OF 16 Elsevier BIOBASE COPYRIGHT 2008 Elsevier Science B.V.  
on STN DUPLICATE

ACCESSION NUMBER: 1996177714 ESBIOBASE <<LOGINID::20080219>>

TITLE: Identification and characterization of the bovine  
herpesvirus 5 US4 gene and gene products

AUTHOR: Engelhardt T.; Keil G.M.

CORPORATE SOURCE: G.M. Keil, Inst. of Molecular/Cellular Virology,  
Friedrich-Loeffler-Institutes, Federal Res. Ctr. Virus  
Dis. Animals, D-17498 Insel Riems, Germany.

SOURCE: Virology, (1996), 225/1 (126-135)

CODEN: VIRLAX ISSN: 0042-6822

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The BHV-5 strain N569 (BHV-5/N569) homolog to the BHV-1 US4 \*\*\*gene\*\*\*

was sequenced and characterized. RNA analyses showed that a 1.8-kb mRNA which contains the BHV-5/N569 US4 open reading frame initiates 55 nucleotides upstream from the predicted translational start codon and terminates 17 nucleotides downstream from the consensus \*\*\*sequence\*\*\* for polyadenylation. Comparison of the deduced amino acid sequences of the predicted US4 encoded proteins of BHV-5/N569 and BHV-1 strain Schonboken (BHV-1/Scho) revealed 75% identity. An antiserum, raised in rabbits after infection with a BHV-5/N569 US4 ORF \*\*\*expressing\*\*\* \*\*\*recombinant\*\*\* vaccinia virus, specifically precipitated a 65-kDa protein and a diffusely migrating protein species with an apparent molecular mass between 90 and >240 kDa from the supernatant of BHV-5/N569 infected cells. Treatment of immunoprecipitated proteins with \*\*\*chondroitinase\*\*\* AC demonstrated that the latter contains glycosaminoglycans. The mobility of the BHV-5/N569 US4 \*\*\*gene\*\*\* products was identical to the BHV-1 US4 CRF encoded \*\*\*glycoprotein\*\*\* G (gG) and glycoproteoglycan G (gpgG; G.M. Keil, T. Engelhardt, A. Karger, and M. Enz, J. Virol. 70, 3032-3038, 1996) and were therefore named BHV-5 gG and BHV-5 gpgG. Immunoprecipitations with sera from BHV-1 infected cattle indicated a type-specific immune response to gG, since these sera failed to react with vaccinia virus- \*\*\*expressed\*\*\* gG5 but recognized vaccinia virus- \*\*\*expressed\*\*\* gG-1.

L7 ANSWER 14 OF 16 BIOTECHNO COPYRIGHT 2008 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1992:22311855 BIOTECHNO <<LOGINID::20080219>>

TITLE: The predominant form of secreted colony stimulating factor-1 is a proteoglycan

AUTHOR: Price L.K.H.; Choi H.U.; Rosenberg L.; Stanley E.R.

CORPORATE SOURCE: Developmental Biology/Cancer Dept., Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461, United States.

SOURCE: Journal of Biological Chemistry, (1992), 267/4 (2190-2199)

CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 1992:22311855 BIOTECHNO <<LOGINID::20080219>>

AB Colony stimulating factor-1 (CSF-1) is a homodimeric \*\*\*glycoprotein\*\*\* that humorally regulates the proliferation and differentiation of mononuclear phagocytic cells and locally regulates cells of the female reproductive tract. Alternative splicing of the human CSF-1 mRNA leads to alternative \*\*\*expression\*\*\* of the CSF-1 homodimer as a secreted \*\*\*glycoprotein\*\*\* or as a membrane-spanning molecule with cell surface biological activity. In the present study, analysis of immunoaffinity-purified CSF-1 from mouse L929 cell medium by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS- PAGE) indicated that CSF-1 is predominantly secreted as highly sulfated species of 375- and 250-kDa with a smaller amount of a 100-kDa species. Analysis by gel filtration in 4 M guanidine HCl buffer, indicated that, in contrast to the 100-kDa species, the highly sulfated species exhibit anomalously high molecular weights and self-association on SDS-PAGE similar to the dermatan sulfate proteoglycan, biglycan. The three predominant CSF-1 species were shown to be an 80-kDa homodimer, an 80-kDa/50-kDa heterodimer, and a 50-kDa homodimer. The 80-kDa subunit contained a single 18-kDa chondroitin sulfate chain that was absent from the 50-kDa subunit. Furthermore, treatment of the 80- and 50-kDa subunits, synthesized in the presence of tunicamycin, with \*\*\*chondroitinase\*\*\* ABC, neuraminidase, and endo-.alpha.- N-acetyl galactosaminidase reduced their apparent molecular masses to 60 and 25 kDa, respectively. These results are consistent with intracellular proteolytic cleavage of the 80-kDa chondroitin sulfate containing subunits from the membrane spanning CSF-1 precursor at a point carboxyl-terminal to the single consensus \*\*\*sequence\*\*\* for glycosaminoglycan addition and cleavage of the 50-kDa \*\*\*glycoprotein\*\*\* subunit at a position aminoterminal to this site. The predominance of the proteoglycan form of secreted CSF-1, which represents only 3-4% of the total trichloroacetic acid-precipitable counts released from .sup.3.sup.5SO.sub.4/.sup.2.sup.--labeled L cells, has important implications for regulation by this growth factor.

L7 ANSWER 15 OF 16 BIOTECHNO COPYRIGHT 2008 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1992:22038035 BIOTECHNO <<LOGINID::20080219>>  
TITLE: Mucin synthesis and secretion in relation in relation

to spontaneous differentiation of colon cancer cells  
in vitro

AUTHOR: Niv Y.; Byrd J.C.; Ho S.B.; Dahiya R.; Kim Y.S.  
CORPORATE SOURCE: GI Research Lab (151M2), VA Medical Center, 4150  
Clement St., San Francisco, CA 94121, United States.

SOURCE: International Journal of Cancer, (1992), 50/1  
(147-152)

CODEN: IJCNAW ISSN: 0020-7136

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 1992:22038035 BIOTECHNO <<LOGINID::20080219>>

AB The synthesis and secretion of mucin-like high-molecular

\*\*\*glycoprotein\*\*\* was studied in 2 human colon cancer cell lines that  
spontaneously differentiate in culture (Caco-2 and T84) and in 2 cell  
lines that do not spontaneously differentiate (LS174T and HT29). Mucin,  
quantitated by .sup.3H-glucosamine labelling and chromatography on  
Sepharose CL-4B was found to be produced by all 4 cell lines. The  
mucinous nature of the labelled high-molecular \*\*\*glycoprotein\*\*\* was  
verified by enzymatic degradation treatments (heparinase, hyaluronidase,  
\*\*\*chondroitinase\*\*\* ABC, and N-glycanase), alkaline-borohydride  
treatment, inhibition of labelling by the glycosylation inhibitor  
benzyl-.alpha.-GalNAc, and by CsCl-density-gradient centrifugation. In  
all 4 cell lines, an inverse correlation of mucin synthesis with cell  
density was demonstrated. In Caco-2 cells, the spontaneous post-confluent  
enterocytic differentiation with increased brush-border enzyme

\*\*\*expression\*\*\* was associated with a decrease in mucin synthesis and  
in the activities of polypeptidyl GalNAc transferase and  
.beta.,1,3-galactosyltransferase activity. Using cDNA probes for 2  
distinct human intestinal mucins (MUC2 and MUC3), we found that all 4  
colon cancer cell lines \*\*\*expressed\*\*\* mucin message, but the types  
of mucin mRNA \*\*\*expressed\*\*\* differed. These data indicate that  
mucin-like glycoproteins can be synthesized by cell lines derived from  
non-mucinous colon cancer, whether or not they undergo spontaneous  
differentiation in culture. These cell lines may serve as in vitro models  
for studying apomucin heterogeneity and control of mucin \*\*\*gene\*\*\*  
\*\*\*expression\*\*\*.

L7 ANSWER 16 OF 16 USPATFULL on STN

ACCESSION NUMBER: 88:50267 USPATFULL <<LOGINID::20080219>>

TITLE: Monoclonal antibodies to cell surface antigens of human  
teratocarcinomas

INVENTOR(S): Rettig, Wolfgang, NY, NY, United States  
Cordon-Cardo, Carlos, NY, NY, United States  
Oettgen, Herbert F., New Canaan, CT, United States  
Old, Lloyd J., New York, NY, United States  
Lloyd, Kenneth O., New York, NY, United States  
Ng, Jennifer, New York, NY, United States

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, New  
York, NY, United States (U.S. corporation)

NUMBER KIND DATE

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PATENT INFORMATION: US 4762800 19880809  
APPLICATION INFO.: US 1984-604080 19840426 (6)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Tarcza, John E.  
LEGAL REPRESENTATIVE: White, John P.  
NUMBER OF CLAIMS: 6  
EXEMPLARY CLAIM: 1,3  
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)  
LINE COUNT: 708  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antibody-producing hybridoma cell lines made by fusion of NS/1 cells  
with spleen cells of mice after immunization with human teratocarcinoma



cells are presented. Monoclonal antibodies from these cell lines recognize the K4, K2 and P12 antigenic systems and are thus useful in detecting and differentiating between normal and cancerous cells. These monoclonal antibodies are especially useful in pathologic analysis of human tumors, especially teratocarcinomas.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L1 QUE CHONDROITINASE

FILE 'BIOSIS, CAPLUS, MEDLINE, EMBASE, SCISEARCH, USPATFULL, ESBIODASE,  
BIOTECHNO, LIFESCI, PASCAL, TOXCENTER, IFIPAT, WPIDS, BIOENG, AGRICOLA'  
ENTERED AT 08:30:42 ON 19 FEB 2008

L2 . 12364 S L1

L3 897 S (GENE OR SEQUENCE OR POLYNUCLEOTIDE OR CONE OR RECOMBINANT) (

L4 308 S EXPRESS? (S) L3

L5 28 S (GLYCOPROTEIN OR GLYCOSYL?)(S) L4

L6 1 S PNGASE AND L5

L7 16 DUP REM L5 (12 DUPLICATES REMOVED)

=> log Y

Biblio. Data	Description	Claims	National Phase	Notices	Documents
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Latest bibliographic data on file with the International Bureau

Publication Number: WO/2004/028479 International Application No.: PCT/US2003/030907  
 Publication Date: 08.04.2004 International Filing Date: 25.09.2003

Int. Class.: **A61K 38/00** (2006.01), **A61K 39/395** (2006.01), **A61K 45/00** (2006.01), **A61P 17/06** (2006.01), **C07K 14/47** (2006.01), **C07K 16/18** (2006.01), **C07K 19/00** (2006.01), **C12N 15/12** (2006.01), **C12P 21/02** (2006.01), **C12Q 1/02** (2006.01), **C12Q 1/68** (2006.01), **G01N 33/53** (2006.01)

Applicants: **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US) (*All Except US*).  
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**JACKMAN, Janet** [US/US]; 94 Patrick Way, Half Moon Bay, CA 94019 (US) (*US Only*).  
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**WOOD, William, I.** [US/US]; 35 Southdown Court, Hillsborough, CA 94010 (US) (*US Only*).  
**WU, Thomas, D.** [US/US]; 41 Nevada Street, San Francisco, CA 94110 (US) (*US Only*).

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Agent: **CARPENTER, David, A.**; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).

Priority Data: 60/414,006 25.09.2002 US

Title: NOUVELLES COMPOSITIONS ET METHODES DE TRAITEMENT DU PSORIASIS

Abstract: La présente invention concerne des compositions contenant une nouvelle protéine ainsi que des méthodes d'utilisation desdites compositions pour le diagnostic et le traitement du psoriasis.

Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.  
 African Regional Intellectual Property Org. (ARIPO) (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW)  
 Eurasian Patent Organization (EAPL) (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)  
 European Patent Office (EPO) (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR)  
 African Intellectual Property Organization (OAPI) (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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# (WO/2004/028479) NOUVELLES COMPOSITIONS ET METHODES DE TRAITEMENT D PSORIASIS

Latest bibliographic data on file with the International Bureau

Publication Number: WO/2004/028479 International Application No.: PCT/US2003/030907

Publication Date: 08.04.2004 International Filing Date: 25.09.2003

Int. Class.: A61K 38/00 (2006.01), A61K 39/395 (2006.01), A61K 45/00 (2006.01), A61P 17/06 (2006.01), C07K 19/00 (2006.01), C07K 15/12 (2006.01), C12N 21/02 (2006.01), C12Q 1/02 (2006.01), G01N 33/53 (2006.01)

Applicants: GENENTECH, INC. [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US) (All Except U)  
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Agent: CARPENTER, David, A.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).

Priority Data: 60/414,006 25.09.2002 US

Title: NOUVELLES COMPOSITIONS ET METHODES DE TRAITEMENT DU PSORIASIS

Abstract: La présente invention concerne des compositions contenant une nouvelle protéine ainsi que des méth compositions pour le diagnostic et le traitement du psoriasis.

**Designated States:** AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, GD, GE, GH, GM, GR, GU, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UG, UY, ZA, ZM, ZW

African Regional Intellectual Property Org. (ARIPO) (GH, GM, KE, LS, MV, MZ, SD, SL, SZ, TZ, UG, ZM)  
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# (WO/2004/028479) NOUVELLES COMPOSITIONS ET METHODES DE TRAITEMENT DE LA PSORIASIS

Note: OCR Text

NOVEL COMPOSITIONS AND METHODS FOR THE TREATMENT OF PSORIASIS Field of the Invention relates to compositions and methods useful for the diagnosis and treatment of psoriasis.

Background of the Invention Immune related and inflammatory diseases are the manifestation or consequence of multiple interconnected biological pathways which in normal physiology are critical to respond to repair from insult or injury, and mount innate and acquired defense against foreign organisms. Diseases these normal physiological pathways cause additional insult or injury either as directly related to the consequence of abnormal regulation or excessive stimulation, as a reaction to self, or as a combinatoric

Though the genesis of these diseases often involves multistep pathways and often multiple different biological intervention at critical points in one or more of these pathways can have an ameliorative or therapeutic intervention can occur by either antagonism of a detrimental process/pathway or stimulation of a beneficial

Many immune related diseases are known and have been extensively studied. Such diseases include inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency, neoplasia, etc.

T lymphocytes (T cells) are an important component of a mammalian immune response. T cells recognize and associated with a self-molecule encoded by genes within the major histocompatibility complex (MHC). Displayed together with MHC molecules on the surface of antigen presenting cells, virus infected cells. The T cell system eliminates these altered cells which pose a health threat to the host mammal. T cell cytotoxic T cells. Helper T cells proliferate extensively following recognition of an antigen-MHC complex. Helper T cells also secrete a variety of cytokines, i.e., lymphokines, which play a central role in the cytotoxic T cells and a variety of other cells which participate in the immune response.

Several diseases of the skin are correlated with an aberrant T cell response and to autoimmunity.

Psoriasis is thought to be an autoimmune disease. Specifically, T-cells of the immune system recognize attack the area where that protein is found, causing the too-rapid growth of new skin cells and painful. These lesions are characterized by hyperproliferation of keratinocytes and the accumulation of activated T-cells of the psoriatic lesions. There are several forms of psoriasis; guttate is the one that most commonly occurs. It is sometimes preceded by an upper respiratory infection. Guttate psoriasis is noncontagious and child-like lesions, usually scattered over the trunk, limbs and scalp. According to the National Psoriasis Foundation, seven million people in the United States have psoriasis. About 20,000 children are diagnosed with psoriasis each year. The cases are attributed to upper respiratory infections. It is estimated that only about 1.5 million people seek treatment, primarily due to lack of or dissatisfaction with current treatments. Although the initial mechanism is unknown, genetic linkages have been mapped to at least 7 psoriasis susceptibility loci (Pso1 on 6p21, Pso2 on 12q13, Pso3 on 17q21, Pso4 on 10q26, Pso5 on 3q21, Pso6 on 19p13, and Pso7 on 1p). Some of these loci overlap with inflammatory diseases including rheumatoid arthritis, atopic dermatitis, and irritable bowel disease. In experiments determine that a gene is upregulated in psoriatic skin vs. normal skin.

Despite the above identified advances in psoriasis research, there is a great need for additional diagnostic methods capable of detecting the presence of a psoriasis in a mammal and for effectively inhibiting this affliction. An objective of the present invention is to identify polypeptides that are overexpressed in psoriasis as compared to normal polypeptides, and their encoding nucleic acids, to produce compositions of matter useful in the diagnosis and diagnostic detection of psoriasis in mammals.

**Summary of the Invention A. Embodiments** The present invention concerns compositions and methods for the treatment of psoriasis in mammals, including humans. The present invention is based on the identification of (including agonist and antagonist antibodies) which are a result of psoriasis in mammals. Immune response in psoriasis may be treated by suppressing the immune response. Molecules that enhance the immune response potentiate the immune response to an antigen. Molecules which stimulate the immune response can lead to where enhancement of the immune response would be beneficial. Alternatively, molecules that suppress the immune response or reduce the immune response to an antigen (e.g., neutralizing antibodies) can be used to attenuate the immune response would be beneficial (e.g., inflammation). Accordingly, the present invention provides antagonists thereof are also useful to prepare medicines and medicaments for the treatment of psoriasis.

In a specific aspect, such medicines and medicaments comprise a therapeutically effective amount of an agonist or antagonist thereof with a pharmaceutically acceptable carrier. Preferably, the admixture is sterile.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a particular antigen comprising contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity of the polypeptide. Preferably, the PRO polypeptide is a native sequence PRO polypeptide. In a specific aspect, the antagonist is an anti-PRO antibody.

In another embodiment, the invention concerns a composition of matter comprising a PRO polypeptide and an antibody which binds the polypeptide in admixture with a carrier or excipient. In one aspect, the composition is therapeutically effective amount of the polypeptide or antibody. In a further aspect, when the composition is an inhibiting molecule, the composition is useful for: (a) reducing the amount of psoriasis tissue of a mammal by inhibiting or reducing an auto-immune response in a mammal in need thereof, in another aspect, the composition is further active ingredient, which may, for example, be a further antibody or a cytotoxic or chemotherapeutic composition is sterile.

In another embodiment, the invention concerns a method of treating psoriasis in a mammal in need thereof by administering to the mammal an effective amount of a PRO polypeptide and an agonist or antagonist thereof.

In another embodiment, the invention provides an antibody which specifically binds to any of the above polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment. In one aspect, the present invention concerns an isolated antibody which binds a PRO polypeptide; the antibody mimics the activity of a PRO polypeptide (an agonist antibody) or conversely the antibody activity of a PRO polypeptide (an antagonist antibody). In another aspect, the antibody is a monoclonal antibody which has nonhuman complementarity determining region (CDR) residues and human framework region (CH) residues. The antibody may be labeled and may be immobilized on a solid support. In a further aspect, the antibody is an anti-idiotype antibody, a single-chain antibody, or an anti-idiotypic antibody.

In yet another embodiment, the present invention provides a composition comprising an anti-PRO antibody and a pharmaceutically acceptable carrier. In one aspect, the composition comprises a therapeutically effective amount of the antibody. Preferably, the composition is sterile. The composition may be administered in the form of a liquid preparation which may be preserved to achieve extended storage stability. Alternatively, the antibody is a monoclonal antibody fragment, a humanized antibody, or a single-chain antibody.

In a further embodiment, the invention concerns an article of manufacture, comprising: (a) a composition comprising a PRO polypeptide or agonist or antagonist thereof; (b) a container containing said composition; and (c) a package insert included in said container referring to the use of said PRO polypeptide or agonist or antagonist thereof in the treatment of an immune related disease. The composition may comprise a therapeutic amount of PRO polypeptide or the agonist or antagonist thereof.

In yet another embodiment, the present invention concerns a method of diagnosing psoriasis in a mammal. The method comprises: (a) determining the level of expression of a gene encoding a PRO polypeptide (a) in a test sample of tissue cells obtained from a mammal; and (b) comparing the level of expression of the gene in the test sample to the level of expression of the gene in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower level of expression in the test sample as compared to the control sample indicates the presence of psoriasis in the mammal from which the test sample were obtained.

In another embodiment, the present invention concerns a method of diagnosing psoriasis in a mammal. The method comprises: (a) determining the level of expression of a gene encoding a PRO polypeptide (a) in a test sample of tissue cells obtained from a mammal; and (b) detecting the presence or absence of said PRO polypeptide, in the test sample; wherein the formation of said complex or absence of said complex indicates the presence or absence of psoriasis, and may be used for monitoring the complex formation in a control sample of known normal tissue cells of the same cell type. The complexes formed in the test sample indicates the presence or absence of psoriasis in the mammal from which the test sample were obtained. The antibody preferably carries a detectable label.

Complex formation can be monitored, for example, by light microscopy, flow cytometry, fluorimetry, or any other suitable method. The test sample is usually obtained from an individual suspected of having psoriasis.

In another embodiment, the invention provides a method for determining the presence of a PRO polypeptide in a sample of cells suspected of containing the PRO polypeptide to an anti-PRO antibody. The method comprises: (a) exposing a test sample of cells suspected of containing the PRO polypeptide to an anti-PRO antibody; and (b) detecting the binding of said antibody to said cell sample. In a specific aspect, the sample comprises a cell suspension of cells suspected of containing the PRO polypeptide. The antibody is preferably detectably labeled and the antibody binds to the cell. The antibody binds to the cell.

In another embodiment, the present invention concerns a psoriasis diagnostic kit, comprising an anti-PRO antibody and a suitable packaging. The kit preferably contains instructions for using the antibody to detect the presence of psoriasis in a sample. Preferably the carrier is pharmaceutically acceptable.

In another embodiment, the present invention concerns a diagnostic kit containing an anti-PRO antibody and a suitable packaging. The kit preferably contains instructions for using the antibody to detect the presence of psoriasis in a sample. Preferably the carrier is pharmaceutically acceptable.







In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence that encodes the same mature polypeptide encoded by any of the human protein cDNAs as a complement of the DNA molecule of (a).

Another aspect of the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence which is either transmembrane domain-deleted or transmembrane domain-inactivated, or encoding nucleotide sequence, wherein the transmembrane domain (s) of such polypeptide are disordered soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complementary use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally comprise a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleotides usually at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160 nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 210 nucleotides in length, alternatively at least about 220 nucleotides in length, alternatively at least about 230 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 260 nucleotides in length, alternatively at least about 270 nucleotides in length, alternatively at least about 280 nucleotides in length, alternatively at least about 290 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 310 nucleotides in length, alternatively at least about 320 nucleotides in length, alternatively at least about 330 nucleotides in length, alternatively at least about 340 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 360 nucleotides in length, alternatively at least about 370 nucleotides in length, alternatively at least about 380 nucleotides in length, alternatively at least about 390 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 410 nucleotides in length, alternatively at least about 420 nucleotides in length, alternatively at least about 430 nucleotides in length, alternatively at least about 440 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 460 nucleotides in length, alternatively at least about 470 nucleotides in length, alternatively at least about 480 nucleotides in length, alternatively at least about 490 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 510 nucleotides in length, alternatively at least about 520 nucleotides in length, alternatively at least about 530 nucleotides in length, alternatively at least about 540 nucleotides in length, alternatively at least about 550 nucleotides in length, alternatively at least about 560 nucleotides in length, alternatively at least about 570 nucleotides in length, alternatively at least about 580 nucleotides in length, alternatively at least about 590 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 610 nucleotides in length, alternatively at least about 620 nucleotides in length, alternatively at least about 630 nucleotides in length, alternatively at least about 640 nucleotides in length, alternatively at least about 650 nucleotides in length, alternatively at least about 660 nucleotides in length, alternatively at least about 670 nucleotides in length, alternatively at least about 680 nucleotides in length, alternatively at least about 690 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 710 nucleotides in length, alternatively at least about 720 nucleotides in length, alternatively at least about 730 nucleotides in length, alternatively at least about 740 nucleotides in length, alternatively at least about 750 nucleotides in length, alternatively at least about 760 nucleotides in length, alternatively at least about 770 nucleotides in length, alternatively at least about 780 nucleotides in length, alternatively at least about 790 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 810 nucleotides in length, alternatively at least about 820 nucleotides in length, alternatively at least about 830 nucleotides in length, alternatively at least about 840 nucleotides in length, alternatively at least about 850 nucleotides in length, alternatively at least about 860 nucleotides in length, alternatively at least about 870 nucleotides in length, alternatively at least about 880 nucleotides in length, alternatively at least about 890 nucleotides in length, alternatively at least about 900 nucleotides in length, alternatively at least about 910 nucleotides in length, alternatively at least about 920 nucleotides in length, alternatively at least about 930 nucleotides in length, alternatively at least about 940 nucleotides in length, alternatively at least about 950 nucleotides in length, alternatively at least about 960 nucleotides in length, alternatively at least about 970 nucleotides in length, alternatively at least about 980 nucleotides in length, alternatively at least about 990 nucleotides in length, alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means nucleotide sequence length plus or minus 10% of that referenced length.

It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequences are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also, polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptides comprising a binding site for an anti-PRO antibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated herein above identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence that encodes the same mature polypeptide encoded by any of the human protein cDNAs as a complement of the DNA molecule of (a).

about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity, having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein, specifically defined fragment of the full-length amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence as disclosed herein, alternatively at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an encoded by any of the human protein cDNAs as disclosed herein.

In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as disclosed herein, alternatively at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an encoded by any of the human protein cDNAs as disclosed herein.

Another aspect of the invention provides an isolated PRO polypeptide which is either a transmembrane protein or a soluble protein. Processes for producing the same are also herein described, which comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid sequence under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide. In particular, the agonist or antagonist is an anti-PRO antibody or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide. The method comprises contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity of the candidate molecule. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, an agonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a disease. The medicament is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

BRIEF DESCRIPTION OF THE DRAWINGS The Figures 1-2484 show the nucleic acids of the invent polypeptides.

Figure 1 shows a nucleotide sequence (SEQ ID NO : 1) of a native sequence PRO83270 cDNA, wher clone designated herein as "DNA326953".

Figure 2 shows the amino acid sequence (SEQ ID NO : 2) derived from the coding sequence of SEQ

Figure 3 shows a nucleotide sequence (SEQ ID NO : 3) of a native sequence PR060747 cDNA, wher designated herein as "DNA272614".

Figure 4 shows the amino acid sequence (SEQ ID NO : 4) derived from the coding sequence of SEQ

Figure 5 shows a nucleotide sequence (SEQ ID NO : 5) of a native sequence PR02690 cDNA, wherei designated herein as "DNA88189".

Figure 6 shows the amino acid sequence (SEQ ID NO : 6) derived from the coding sequence of SEQ

Figure 7 shows a nucleotide sequence (SEQ ID NO : 7) of a native sequence PR061604 cDNA, wher designated herein as "DNA272992".

Figure 8 shows the amino acid sequence (SEQ ID NO : 8) derived from the coding sequence of SEQ

Figure 9A-B shows a nucleotide sequence (SEQ ID NO : 9) of a native sequence PR083571 cDNA, w clone designated herein as "DNA327520".

Figure 10 shows the amino acid sequence (SEQ ID NO : 10) derived from the coding sequence of SE 9A-B.

Figure 11 shows a nucleotide sequence (SEQ ID NO : 11) of a native sequence PR058320 cDNA, wh clone designated herein as "DNA327521".

Figure 12 shows the amino acid sequence (SEQ ID NO : 12) derived from the coding sequence of SE Figure 11.

Figure 13 shows a nucleotide sequence (SEQ ID NO : 13) of a native sequence PR02874 cDNA, whe clone designated herein as "DNA327522".

Figure 14 shows the amino acid sequence (SEQ ID NO : 14) derived from the coding sequence of SE Figure 13.

Figure 15A-B shows a nucleotide sequence (SEQ ID NO : 15) of a native sequence PR049240 cDNA a clone designated herein as "DNA254177".

Figure 15A-B.

Figure 17 shows a nucleotide sequence (SEQ ID NO : 17) of a native sequence PRO59307 cDNA, wh clone designated herein as "DNA270977".

Figure 18 shows the amino acid sequence (SEQ ID NO : 18) derived from the coding sequence of SE Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO : 19) of a native sequence PR04619 cDNA, wh clone designated herein as "DNA103298".

Figure 20 shows the amino acid sequence (SEQ ID NO : 20) derived from the coding sequence of SE Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO : 21) of a native sequence PR038028 cDNA, wh clone designated herein as "DNA327523".

Figure 22 shows the amino acid sequence (SEQ ID NO : 22) derived from the coding sequence of SE Figure 21.

Figure 23A-B shows a nucleotide sequence (SEQ ID NO : 23) of a native sequence PR083572 cDNA a clone designated herein as "DNA327524".

Figure 24 shows the amino acid sequence (SEQ ID NO : 24) derived from the coding sequence of SE Figure 23A-B.

Figure 25 shows a nucleotide sequence (SEQ ID NO : 25) of a native sequence PR02065 cDNA, wh clone designated herein as "DNA326839".

Figure 26 shows the amino acid sequence (SEQ ID NO : 26) derived from the coding sequence of SE Figure 25.

Figure 27A-C shows a nucleotide sequence (SEQ ID NO : 27) of a native sequence PRO83573 cDNA a clone designated herein as "DNA327525".

Figure 28 shows the amino acid sequence (SEQ ID NO : 28) derived from the coding sequence of SE Figure 27A-C.

Figure 29 shows a nucleotide sequence (SEQ ID NO : 29) of a native sequence PR083574 cDNA, wh clone designated herein as "DNA327526".

Figure 30 shows the amino acid sequence (SEQ ID NO : 30) derived from the coding sequence of SE Figure 29.

Figure 31 shows a nucleotide sequence (SEQ ID NO : 31) of a native sequence PR083575 cDNA, wh clone designated herein as "DNA327527".

Figure 32 shows the amino acid sequence (SEQ ID NO : 32) derived from the coding sequence of SE Figure 31.

Figure 33A-B shows a nucleotide sequence (SEQ ID NO : 33) of a native sequence PR083576 cDNA a clone designated herein as "DNA327528".

Figure 34 shows the amino acid sequence (SEQ ID NO : 34) derived from the coding sequence of SE Figure 33A-B.

Figure 35 shows a nucleotide sequence (SEQ ID NO : 35) of a native sequence PRO83577 cDNA, wt clone designated herein as "DNA327529".

Figure 36 shows the amino acid sequence (SEQ ID NO : 36) derived from the coding sequence of SE Figure 35.

Figure 37 shows a nucleotide sequence (SEQ ID NO : 37) of a native sequence PR083578 cDNA, wh clone designated herein as "DNA327530".

Figure 38 shows the amino acid sequence (SEQ ID NO : 38) derived from the coding sequence of SE Figure 37.

Figure 39 shows a nucleotide sequence (SEQ ID NO : 39) of a native sequence PRO12077 cDNA, wt clone designated herein as "DNA324468".

Figure 40 shows the amino acid sequence (SEQ ID NO : 40) derived from the coding sequence of SE Figure 39.

Figure 41 shows a nucleotide sequence (SEQ ID NO : 41) of a native sequence PRO83579 cDNA, wt clone designated herein as "DNA327531".

Figure 42 shows the amino acid sequence (SEQ ID NO : 42) derived from the coding sequence of SE Figure 41.

Figure 42 shows a nucleotide sequence (SEQ ID NO : 42) of a native sequence PR071901 cDNA, wh clone designated herein as "DNA325124".

Figure 43 shows the amino acid sequence (SEQ ID NO : 43) derived from the coding sequence of SE Figure 44.

Figure 45 shows a nucleotide sequence (SEQ ID NO : 45) of a native sequence PR071134 cDNA, wh clone designated herein as "DNA327532".

Figure 46 shows the amino acid sequence (SEQ ID NO : 46) derived from the coding sequence of SE Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO : 47) of a native sequence PR036526 cDNA, wh

clone designated herein as "DNA327533".

Figure 48 shows the amino acid sequence (SEQ ID NO : 48) derived from the coding sequence of SE Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO : 49) of a native sequence PR062529 cDNA, wh clone designated herein as "DNA274759".

Figure 50 shows the amino acid sequence (SEQ ID NO : 50) derived from the coding sequence of SE Figure.

Figure 51 shows a nucleotide sequence (SEQ ID NO : 51) of a native sequence PR062782 cDNA, wh clone designated herein as "DNA275062".

Figure 52 shows the amino acid sequence (SEQ ID NO : 52) derived from the coding sequence of SE Figure 51.

Figure 53 shows a nucleotide sequence (SEQ ID NO : 53) of a native sequence PR02758 cDNA, wh clone designated herein as "DNA88350".

Figure 54 shows the amino acid sequence (SEQ ID NO : 54) derived from the coding sequence of SE Figure 53.

Figure 55A-B shows a nucleotide sequence (SEQ ID NO : 55) of a native sequence PR041180 cDNA a clone designated herein as "DNA327534".

Figure 56 shows the amino acid sequence (SEQ ID NO : 56) derived from the coding sequence of SE Figure 55A-B.

Figure 57 shows a nucleotide sequence (SEQ ID NO : 57) of a native sequence PR039268 cDNA, wh clone designated herein as "DNA287207".

Figure 58 shows the amino acid sequence (SEQ ID NO : 58) derived from the coding sequence of SE Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO : 59) of a native sequence PR083580 cDNA, wh clone designated herein as "DNA327535".

Figure 60 shows the amino acid sequence (SEQ ID NO : 60) derived from the coding sequence of SE Figure 59.

Figure 61 shows a nucleotide sequence (SEQ ID NO : 61) of a native sequence PR059895 cDNA, wh clone designated herein as "DNA271608".

Figure 62 shows the amino acid sequence (SEQ ID NO : 62) derived from the coding sequence of SE Figure 61.

Figure 63A-B shows a nucleotide sequence (SEQ ID NO : 63) of a native sequence PR037003 cDNA a clone designated herein as "DNA327536".

Figure 64 shows the amino acid sequence (SEQ ID NO : 64) derived from the coding sequence of SE Figure 63A-B.

Figure 65 shows a nucleotide sequence (SEQ ID NO : 65) of a native sequence PR03344 cDNA, wh clone designated herein as "DNA196817".

Figure 66 shows the amino acid sequence (SEQ ID NO : 66) derived from the coding sequence of SE Figure 65.

Figure 67A-B shows a nucleotide sequence (SEQ ID NO : 67) of a native sequence PRO83581 cDNA a clone designated herein as "DNA327537".

Figure 68 shows the amino acid sequence (SEQ ID NO : 68) derived from the coding sequence of SE Figure 67A-B.

Figure 69 shows a nucleotide sequence (SEQ ID NO : 69) of a native sequence PR010315 cDNA, wh clone designated herein as "DNA327538".

Figure 70 shows the amino acid sequence (SEQ ID NO : 70) derived from the coding sequence of SE Figure 69.

Figure 71A-B shows a nucleotide sequence (SEQ ID NO : 71) of a native sequence PRO12211 cDNA a clone designated herein as "DNA327539".

Figure 72 shows the amino acid sequence (SEQ ID NO : 72) derived from the coding sequence of SE Figure 71A-B.

Figure 73 shows a nucleotide sequence (SEQ ID NO : 73) of a native sequence PR036587 cDNA, wh clone designated herein as "DNA226124".

Figure 74 shows the amino acid sequence (SEQ ID NO : 74) derived from the coding sequence of SE Figure 73.

Figure 75 shows a nucleotide sequence (SEQ ID NO : 75) of a native sequence PR037082 cDNA, wh clone designated herein as "DNA226619".

Figure 76 shows the amino acid sequence (SEQ ID NO : 76) derived from the coding sequence of SE Figure 75.

Figure 77 shows a nucleotide sequence (SEQ ID NO : 77) of a native sequence PR037540 cDNA, wh clone designated herein as "DNA227077".

Figure 78 shows the amino acid sequence (SEQ ID NO : 78) derived from the coding sequence of SE



Figure 77.

Figure 79 shows a nucleotide sequence (SEQ ID NO : 79) of a native sequence PR038005 cDNA, wh clone designated herein as "DNA327540".

Figure 80 shows the amino acid sequence (SEQ ID NO : 80) derived from the coding sequence of SE Figure 79.

Figure 81 shows a nucleotide sequence (SEQ ID NO : 81) of a native sequence PR036341 cDNA, wh clone designated herein as "DNA225878".

Figure 80 shows the amino acid sequence (SEQ ID NO : 80) derived from the coding sequence of SE Figure 81.

Figure 83 shows a nucleotide sequence (SEQ ID NO : 83) of a native sequence PR060864 cDNA, wh clone designated herein as "DNA272753".

Figure 84 shows the amino acid sequence (SEQ ID NO : 84) derived from the coding sequence of SE Figure 83.

Figure 85 shows a nucleotide sequence (SEQ ID NO : 85) of a native sequence PR071139 cDNA, wh clone designated herein as "DNA304713".

Figure 86 shows the amino acid sequence (SEQ ID NO : 86) derived from the coding sequence of SE Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO : 87) of a native sequence PR060225 cDNA, wh clone designated herein as "DNA298609".

Figure 88 shows the amino acid sequence (SEQ ID NO : 88) derived from the coding sequence of SE Figure 87.

Figure 89 shows a nucleotide sequence (SEQ ID NO : 89) of a native sequence PR071267 cDNA, wh clone designated herein as "DNA304872".

Figure 90 shows the amino acid sequence (SEQ ID NO : 90) derived from the coding sequence of SE Figure 89.

Figure 91 shows a nucleotide sequence (SEQ ID NO : 91) of a native sequence PR082678 cDNA, wh clone designated herein as "DNA326273".

Figure 92 shows the amino acid sequence (SEQ ID NO : 92) derived from the coding sequence of SE Figure 91.

Figure 93A-B shows a nucleotide sequence (SEQ ID NO : 93) of a native sequence PR02672 cDNA, clone designated herein as "DNA326191".

Figure 94 shows the amino acid sequence (SEQ ID NO : 94) derived from the coding sequence of S Figure 93.

Figure 95A-B shows a nucleotide sequence (SEQ ID NO : 95) of a native sequence PR02621 cDNA clone designated herein as "DNA327541".

Figure 96 shows the amino acid sequence (SEQ ID NO : 96) derived from the coding sequence of S Figure 95A-B.

Figure 97 shows a nucleotide sequence (SEQ ID NO : 97) of a native sequence PRO12890 cDNA v clone designated herein as "DNA151802".

Figure 98 shows the amino acid sequence (SEQ ID NO : 98) derived from the coding sequence of S Figure 97.

Figure 99 shows a nucleotide sequence (SEQ ID NO : 99) of a native sequence PR060221 cDNA, w clone designated herein as "DNA271945".

Figure 100 shows the amino acid sequence (SEQ ID NO : 100) derived from the coding sequence of Figure 99.

Figure 101 shows a nucleotide sequence (SEQ ID NO : 101) of a native sequence PR039294 cDNA a clone designated herein as "DNA239053".

Figure 102 shows the amino acid sequence (SEQ ID NO : 102) derived from the coding sequence of Figure 101.

Figure 103 shows a nucleotide sequence (SEQ ID NO : 103) of a native sequence PR083582 cDNA a clone designated herein as "DNA327542".

Figure 104 shows the amino acid sequence (SEQ ID NO : 104) derived from the coding sequence of Figure 103.

Figure 105 shows a nucleotide sequence (SEQ ID NO : 105) of a native sequence PR080554 cDNA a clone designated herein as "DNA323805".

Figure 106 shows the amino acid sequence (SEQ ID NO : 106) derived from the coding sequence of Figure 105.

Figure 107 shows a nucleotide sequence (SEQ ID NO : 107) of a native sequence PR062241 cDNA a clone designated herein as "DNA327543".

Figure 108 shows the amino acid sequence (SEQ ID NO : 108) derived from the coding sequence of Figure 107.

Figure 109 shows a nucleotide sequence (SEQ ID NO : 109) of a native sequence PR070357 cDNA

a clone designated herein as "DNA327544".

Figure 108 shows the amino acid sequence (SEQ ID NO : 108) derived from the coding sequence of Figure 109.

Figure 111A-B shows a nucleotide sequence (SEQ ID NO : 111) of a native sequence PR082731 cD 111 is a clone designated herein as "DNA327545".

Figure 112 shows the amino acid sequence (SEQ ID NO : 112) derived from the coding sequence of Figure 111A-B.

Figure 113 shows a nucleotide sequence (SEQ ID NO : 113) of a native sequence cDNA, wherein SE designated herein as "DNA327546".

Figure 114 shows a nucleotide sequence (SEQ ID NO : 114) of a native sequence PR083583 cDNA, a clone designated herein as "DNA327547".

Figure 115 shows the amino acid sequence (SEQ ID NO : 115) derived from the coding sequence of Figure 114.

Figure 116 shows a nucleotide sequence (SEQ ID NO : 116) of a native sequence PRO12618 cDNA, a clone designated herein as "DNA151148".

Figure 117 shows the amino acid sequence (SEQ ID NO : 117) derived from the coding sequence of Figure 116.

Figure 118 shows a nucleotide sequence (SEQ ID NO : 118) of a native sequence PR081281 cDNA, a clone designated herein as "DNA327548".

Figure 119 shows the amino acid sequence (SEQ ID NO : 119) derived from the coding sequence of Figure 118.

Figure 120A-B shows a nucleotide sequence (SEQ ID NO : 120) of a native sequence PR083584 cD 120 is a clone designated herein as "DNA327549".

Figure 121 shows the amino acid sequence (SEQ ID NO : 121) derived from the coding sequence of Figure 120A-B.

Figure 122 shows a nucleotide sequence (SEQ ID NO : 122) of a native sequence PR081164 cDNA, a clone designated herein as "DNA327550".

Figure 123 shows the amino acid sequence (SEQ ID NO : 123) derived from the coding sequence of Figure 122.

Figure 124A-B shows a nucleotide sequence (SEQ ID NO : 124) of a native sequence PR04797 cDNA is a clone designated herein as "DNA103470".

Figure 125 shows the amino acid sequence (SEQ ID NO : 125) derived from the coding sequence of Figure 124.

Figure 126 shows a nucleotide sequence (SEQ ID NO : 126) of a native sequence PR04650 cDNA, a clone designated herein as "DNA103320".

Figure 127 shows the amino acid sequence (SEQ ID NO : 127) derived from the coding sequence of Figure 126.

Figure 128 shows a nucleotide sequence (SEQ ID NO : 128) of a native sequence PR059289 cDNA, a clone designated herein as "DNA327551".

Figure 129 shows the amino acid sequence (SEQ ID NO : 129) derived from the coding sequence of Figure 128.

Figure 130 shows a nucleotide sequence (SEQ ID NO : 130) of a native sequence PR022664 cDNA, a clone designated herein as "DNA327552".

Figure 131 shows the amino acid sequence (SEQ ID NO : 131) derived from the coding sequence of Figure 130.

Figure 132 shows a nucleotide sequence (SEQ ID NO : 132) of a native sequence PR02679 cDNA, a clone designated herein as "DNA88166".

Figure 133 shows the amino acid sequence (SEQ ID NO : 133) derived from the coding sequence of Figure 132.

Figure 134 shows a nucleotide sequence (SEQ ID NO : 134) of a native sequence PR037073 cDNA, a clone designated herein as "DNA304459".

Figure 135 shows the amino acid sequence (SEQ ID NO : 135) derived from the coding sequence of Figure 134.

Figure 136 shows a nucleotide sequence (SEQ ID NO : 136) of a native sequence PR037073 cDNA, a clone designated herein as "DNA304459".

Figure 137 shows the amino acid sequence (SEQ ID NO : 137) derived from the coding sequence of Figure 136.

Figure 138A-B shows a nucleotide sequence (SEQ ID NO : 138) of a native sequence PR083585 cDNA, a clone designated herein as "DNA327553".

Figure 139 shows the amino acid sequence (SEQ ID NO : 139) derived from the coding sequence of Figure 138A-B.

Figure 140 shows a nucleotide sequence (SEQ ID NO : 140) of a native sequence PR059386 cDNA,

a clone designated herein as "DNA327554".

Figure 141 shows the amino acid sequence (SEQ ID NO : 141) derived from the coding sequence of Figure 140.

Figure 142 shows a nucleotide sequence (SEQ ID NO : 142) of a native sequence PRO83586 cDNA, a clone designated herein as "DNA327555".

Figure 143 shows the amino acid sequence (SEQ ID NO : 143) derived from the coding sequence of Figure 142.

Figure 144 shows a nucleotide sequence (SEQ ID NO : 144) of a native sequence PRO2551 cDNA, a clone designated herein as "DNA79129".

Figure 145 shows the amino acid sequence (SEQ ID NO : 145) derived from the coding sequence of Figure 144.

Figure 146 shows a nucleotide sequence (SEQ ID NO : 146) of a native sequence PRO83587 cDNA, a clone designated herein as "DNA327556".

Figure 147 shows the amino acid sequence (SEQ ID NO : 147) derived from the coding sequence of Figure 146.

Figure 148 shows a nucleotide sequence (SEQ ID NO : 148) of a native sequence PRO2804 cDNA, a clone designated herein as "DNA88464".

Figure 149 shows the amino acid sequence (SEQ ID NO : 149) derived from the coding sequence of Figure 148.

Figure 150 shows a nucleotide sequence (SEQ ID NO : 150) of a native sequence PRO62244 cDNA, a clone designated herein as "DNA274326".

Figure 151 shows the amino acid sequence (SEQ ID NO : 151) derived from the coding sequence of Figure 150.

Figure 152A-B shows a nucleotide sequence (SEQ ID NO : 152) of a native sequence PR037659 cDI 152 is a clone designated herein as "DNA227196".

Figure 153 shows the amino acid sequence (SEQ ID NO : 153) derived from the coding sequence of Figure 152A-B.

Figure 154 shows a nucleotide sequence (SEQ ID NO : 154) of a native sequence PR050473 cDNA, a clone designated herein as "DNA255406".

Figure 155 shows the amino acid sequence (SEQ ID NO : 155) derived from the coding sequence of Figure 154.

Figure 156 shows a nucleotide sequence (SEQ ID NO : 156) of a native sequence PRO83588 cDNA, a clone designated herein as "DNA327557".

Figure 157 shows the amino acid sequence (SEQ ID NO : 157) derived from the coding sequence of Figure 156.

Figure 158A-B shows a nucleotide sequence (SEQ ID NO : 158) of a native sequence PRO12515 cD 158 is a clone designated herein as "DNA327558".

Figure 159 shows the amino acid sequence (SEQ ID NO : 159) derived from the coding sequence of Figure 158A-B.

Figure 160 shows a nucleotide sequence (SEQ ID NO : 160) of a native sequence PRO70353 cDNA, a clone designated herein as "DNA290244".

Figure 161 shows the amino acid sequence (SEQ ID NO : 161) derived from the coding sequence of Figure 160.

Figure 162 shows a nucleotide sequence (SEQ ID NO : 162) of a native sequence PRO70329 cDNA, a clone designated herein as "DNA290232".

Figure 163 shows the amino acid sequence (SEQ ID NO : 163) derived from the coding sequence of Figure 162.

Figure 164A-B shows a nucleotide sequence (SEQ ID NO : 164) of a native sequence PRO12561 cD 164 is a clone designated herein as "DNA150966".

Figure 165 shows the amino acid sequence (SEQ ID NO : 165) derived from the coding sequence of Figure 164A-B.

Figure 166 shows a nucleotide sequence (SEQ ID NO : 166) of a native sequence PRO38039 cDNA, a clone designated herein as "DNA227576".

Figure 167 shows the amino acid sequence (SEQ ID NO : 167) derived from the coding sequence of Figure 166.

Figure 168 shows a nucleotide sequence (SEQ ID NO : 168) of a native sequence PRO12769 cDNA, a clone designated herein as "DNA150429".

Figure 169 shows the amino acid sequence (SEQ ID NO : 169) derived from the coding sequence of Figure 168.

Figure 170 shows a nucleotide sequence (SEQ ID NO : 170) of a native sequence PRO83589 cDNA, a clone designated herein as "DNA327559".

Figure 171 shows the amino acid sequence (SEQ ID NO : 171) derived from the coding sequence of

Figure 170.

Figure 172 shows a nucleotide sequence (SEQ ID NO : 172) of a native sequence PRO83590 cDNA, a clone designated herein as "DNA327560".

Figure 173 shows the amino acid sequence (SEQ ID NO : 173) derived from the coding sequence of Figure 172.

Figure 174 shows a nucleotide sequence (SEQ ID NO : 174) of a native sequence PRO80735 cDNA, a clone designated herein as "DNA324015".

Figure 175 shows the amino acid sequence (SEQ ID NO : 175) derived from the coding sequence of Figure 174.

Figure 176 shows a nucleotide sequence (SEQ ID NO : 176) of a native sequence PRO36393 cDNA, a clone designated herein as "DNA225930".

Figure 177 shows the amino acid sequence (SEQ ID NO : 177) derived from the coding sequence of Figure 176.

Figure 178 shows a nucleotide sequence (SEQ ID NO : 178) of a native sequence PRO2842 cDNA, a clone designated herein as "DNA88562".

Figure 179 shows the amino acid sequence (SEQ ID NO : 179) derived from the coding sequence of Figure 178.

Figure 180 shows a nucleotide sequence (SEQ ID NO : 180) of a native sequence PRO81669 cDNA, a clone designated herein as "DNA325092".

Figure 181 shows the amino acid sequence (SEQ ID NO : 181) derived from the coding sequence of Figure 180.

Figure 182 shows a nucleotide sequence (SEQ ID NO : 182) of a native sequence PRO49181 cDNA, a clone designated herein as "DNA253582".

Figure 183 shows the amino acid sequence (SEQ ID NO : 183) derived from the coding sequence of Figure 182.

Figure 184A-B shows a nucleotide sequence (SEQ ID NO : 184) of a native sequence PR083591 cDNA, 184 is a clone designated herein as "DNA327561".

Figure 185 shows the amino acid sequence (SEQ ID NO : 185) derived from the coding sequence of Figure 184A-B.

Figure 186 shows a nucleotide sequence (SEQ ID NO : 186) of a native sequence PRO63048 cDNA, a clone designated herein as "DNA275385".

Figure 187 shows the amino acid sequence (SEQ ID NO : 187) derived from the coding sequence of Figure 186.

Figure 188 shows a nucleotide sequence (SEQ ID NO : 188) of a native sequence PRO50067 cDNA, a clone designated herein as "DNA254978".

Figure 189 shows the amino acid sequence (SEQ ID NO : 189) derived from the coding sequence of Figure 188.

Figure 190 shows a nucleotide sequence (SEQ ID NO : 190) of a native sequence PRO62097 cDNA, a clone designated herein as "DNA274167".

Figure 191 shows the amino acid sequence (SEQ ID NO : 191) derived from the coding sequence of Figure 190.

Figure 192A-B shows a nucleotide sequence (SEQ ID NO : 192) of a native sequence cDNA, whereir designated herein as "DNA327562".

Figure 193 shows a nucleotide sequence (SEQ ID NO : 193) of a native sequence PRO80761 cDNA, a clone designated herein as "DNA324044".

Figure 194 shows the amino acid sequence (SEQ ID NO : 194) derived from the coding sequence of Figure 193.

Figure 195A-B shows a nucleotide sequence (SEQ ID NO : 195) of a native sequence PRO83592 cD 195 is a clone designated herein as "DNA327563".

Figure 196 shows the amino acid sequence (SEQ ID NO : 196) derived from the coding sequence of Figure 195A-B.

Figure 197 shows a nucleotide sequence (SEQ ID NO : 197) of a native sequence PRO12452 cDNA, a clone designated herein as "DNA150757".

- Figure 198 shows the amino acid sequence (SEQ ID NO : 198) derived from the coding sequence of Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO : 199) of a native sequence PRO83593 cDNA, a clone designated herein as "DNA327564".

Figure 200 shows the amino acid sequence (SEQ ID NO : 200) derived from the coding sequence of Figure 199.

Figure 201A-B shows a nucleotide sequence (SEQ ID NO : 201) of a native sequence PRO59326 cDI 201 is a clone designated herein as "DNA270997".

Figure 202 shows the amino acid sequence (SEQ ID NO : 202) derived from the coding sequence of



Figure 201A-B.

Figure 203A-B shows a nucleotide sequence (SEQ ID NO : 203) of a native sequence PRO83594 cDNA, a clone designated herein as "DNA327565".

Figure 204 shows the amino acid sequence (SEQ ID NO : 204) derived from the coding sequence of Figure 203A-B.

Figure 205A-B shows a nucleotide sequence (SEQ ID NO : 205) of a native sequence PRO83595 cDNA, a clone designated herein as "DNA327566".

Figure 206 shows the amino acid sequence (SEQ ID NO : 206) derived from the coding sequence of Figure 205A-B.

Figure 207A-B shows a nucleotide sequence (SEQ ID NO : 207) of a native sequence PR036454 cDNA, a clone designated herein as "DNA225991".

Figure 208 shows the amino acid sequence (SEQ ID NO : 208) derived from the coding sequence of Figure 207A-B.

Figure 209 shows a nucleotide sequence (SEQ ID NO : 209) of a native sequence PR083596 cDNA, a clone designated herein as "DNA327567".

Figure 210 shows the amino acid sequence (SEQ ID NO : 210) derived from the coding sequence of Figure 209.

Figure 211 shows a nucleotide sequence (SEQ ID NO : 211) of a native sequence PR036579 cDNA, a clone designated herein as "DNA226116".

Figure 212 shows the amino acid sequence (SEQ ID NO : 212) derived from the coding sequence of Figure 211.

Figure 213A-B shows a nucleotide sequence (SEQ ID NO : 213) of a native sequence PR058096 cDNA, a clone designated herein as "DNA269686".

Figure 214 shows the amino acid sequence (SEQ ID NO : 214) derived from the coding sequence of Figure 213A-B.

Figure 215 shows a nucleotide sequence (SEQ ID NO : 215) of a native sequence PR057922 cDNA, a clone designated herein as "DNA327568".

Figure 216 shows the amino acid sequence (SEQ ID NO : 216) derived from the coding sequence of Figure 215.

Figure 217 shows a nucleotide sequence (SEQ ID NO : 217) of a native sequence PR02683 cDNA, a clone designated herein as "DNA327569".

Figure 218 shows the amino acid sequence (SEQ ID NO : 218) derived from the coding sequence Figure 217.

Figure 219 shows a nucleotide sequence (SEQ ID NO : 219) of a native sequence cDNA, wherein designated herein as "DNA327570".

Figure 220 shows a nucleotide sequence (SEQ ID NO : 220) of a native sequence PR04735 cDNA clone designated herein as "DNA327571".

Figure 221 shows the amino acid sequence (SEQ ID NO : 221) derived from the coding sequence Figure 220.

Figure 222 shows a nucleotide sequence (SEQ ID NO : 222) of a native sequence PR07143 cDNA clone designated herein as "DNA129504".

Figure 223 shows the amino acid sequence (SEQ ID NO : 223) derived from the coding sequence Figure 222.

Figure 224A-B shows a nucleotide sequence (SEQ ID NO : 224) of a native sequence PRO83597 224 is a clone designated herein as "DNA327572".

Figure 225 shows the amino acid sequence (SEQ ID NO : 225) derived from the coding sequence Figure 225A-B.

Figure 226 shows a nucleotide sequence (SEQ ID NO : 226) of a native sequence PRO81058 cDN 81058 is a clone designated herein as "DNA324392".

Figure 227 shows the amino acid sequence (SEQ ID NO : 227) derived from the coding sequence Figure 226.

Figure 228 shows a nucleotide sequence (SEQ ID NO : 228) of a native sequence PR059301 cDN a clone designated herein as "DNA327573".

Figure 229 shows the amino acid sequence (SEQ ID NO : 229) derived from the coding sequence Figure 228.

Figure 230 shows a nucleotide sequence (SEQ ID NO : 230) of a native sequence PRO12878 cDN a clone designated herein as "DNA325477".

Figure 231 shows the amino acid sequence (SEQ ID NO : 231) derived from the coding sequence Figure 230.

Figure 232 shows a nucleotide sequence (SEQ ID NO : 232) of a native sequence PR070994 cDN a clone designated herein as "DNA302021".

Figure 233 shows the amino acid sequence (SEQ ID NO : 233) derived from the coding sequence

Figure 232.

Figure 234 shows a nucleotide sequence (SEQ ID NO : 234) of a native sequence PRO82546 cDNA, a clone designated herein as "DNA326120".

Figure 235 shows the amino acid sequence (SEQ ID NO : 235) derived from the coding sequence of Figure 234.

Figure 236 shows a nucleotide sequence (SEQ ID NO : 236) of a native sequence PRO12478 cDNA, a clone designated herein as "DNA150808".

Figure 237 shows the amino acid sequence (SEQ ID NO : 237) derived from the coding sequence of Figure 236.

Figure 238 shows a nucleotide sequence (SEQ ID NO : 238) of a native sequence PRO59035 cDNA, a clone designated herein as "DNA270669".

Figure 239 shows the amino acid sequence (SEQ ID NO : 239) derived from the coding sequence of Figure 238.

Figure 240A-D shows a nucleotide sequence (SEQ ID NO : 240) of a native sequence PRO83598 cD 240 is a clone designated herein as "DNA327574".

Figure 241 shows the amino acid sequence (SEQ ID NO : 241) derived from the coding sequence of Figure 240A-D.

Figure 242 shows a nucleotide sequence (SEQ ID NO : 242) of a native sequence PRO50174 cDNA, a clone designated herein as "DNA255088".

Figure 243 shows the amino acid sequence (SEQ ID NO : 243) derived from the coding sequence of Figure 242.

Figure 244A-B shows a nucleotide sequence (SEQ ID NO : 244) of a native sequence PRO83599 cD 244 is a clone designated herein as "DNA327575".

Figure 245 shows the amino acid sequence (SEQ ID NO : 245) derived from the coding sequence of Figure 244A-B.

Figure 246 shows a nucleotide sequence (SEQ ID NO : 246) of a native sequence PRO81689 cDNA, a clone designated herein as "DNA325115".

Figure 247 shows the amino acid sequence (SEQ ID NO : 247) derived from the coding sequence of Figure 246.

Figure 248 shows a nucleotide sequence (SEQ ID NO : 248) of a native sequence PRO83470 cDNA, a clone designated herein as "DNA327193".

Figure 249 shows the amino acid sequence (SEQ ID NO : 249) derived from the coding sequence of Figure 248.

Figure 250 shows a nucleotide sequence (SEQ ID NO : 250) of a native sequence PR058880 cDNA, a clone designated herein as "DNA270502".

Figure 251 shows the amino acid sequence (SEQ ID NO : 251) derived from the coding sequence of Figure 250.

Figure 252 shows a nucleotide sequence (SEQ ID NO : 252) of a native sequence PRO12569 cDNA, a clone designated herein as "DNA150989".

Figure 253 shows the amino acid sequence (SEQ ID NO : 253) derived from the coding sequence of Figure 252.

Figure 254 shows a nucleotide sequence (SEQ ID NO : 254) of a native sequence PR037584 cDNA, a clone designated herein as "DNA227121".

Figure 255 shows the amino acid sequence (SEQ ID NO : 255) derived from the coding sequence of Figure 254.

Figure 256A-B shows a nucleotide sequence (SEQ ID NO : 256) of a native sequence PRO83600 cDNA, a clone designated herein as "DNA327576".

Figure 257 shows the amino acid sequence (SEQ ID NO : 257) derived from the coding sequence of Figure 256A-B.

Figure 258 shows a nucleotide sequence (SEQ ID NO : 258) of a native sequence PR058089 cDNA, a clone designated herein as "DNA269678".

Figure 259 shows the amino acid sequence (SEQ ID NO : 259) derived from the coding sequence of Figure 258.

Figure 260 shows a nucleotide sequence (SEQ ID NO : 260) of a native sequence PR038852 cDNA, a clone designated herein as "DNA234442".

Figure 261 shows the amino acid sequence (SEQ ID NO : 261) derived from the coding sequence of Figure 260.

Figure 262A-B shows a nucleotide sequence (SEQ ID NO : 262) of a native sequence PR061835 cDNA, a clone designated herein as "DNA273879".

Figure 263 shows the amino acid sequence (SEQ ID NO : 263) derived from the coding sequence of Figure 262A-B. Figure 264 shows a nucleotide sequence (SEQ ID NO : 264) of a native sequence PR ID NO : 264 is a clone designated herein as "DNA327577".

Figure 265 shows the amino acid sequence (SEQ ID NO : 265) derived from the coding sequence of SEQ ID NO : 265. Figure 264.

Figure 266A-B shows a nucleotide sequence (SEQ ID NO : 266) of a native sequence PR062605 cDNA. Figure 266 is a clone designated herein as "DNA274852".

Figure 267 shows the amino acid sequence (SEQ ID NO : 267) derived from the coding sequence of : Figure 266A-B.

Figure 268A-B shows a nucleotide sequence (SEQ ID NO : 268) of a native sequence PR062271 cDNA. Figure 268 is a clone designated herein as "DNA327578".

Figure 269 shows the amino acid sequence (SEQ ID NO : 269) derived from the coding sequence of : Figure 268A-B.

Figure 270A-C shows a nucleotide sequence (SEQ ID NO : 270) of a native sequence cDNA, whereir designated herein as "DNA327579".

Figure 271 shows a nucleotide sequence (SEQ ID NO : 271) of a native sequence PR083257 cDNA, a clone designated herein as "DNA326939".

Figure 272 shows the amino acid sequence (SEQ ID NO : 272) derived from the coding sequence of SEQ ID NO : 272. Figure 271.

Figure 273 shows a nucleotide sequence (SEQ ID NO : 273) of a native sequence PR080657 cDNA, a clone designated herein as "DNA323923".

Figure 274 shows the amino acid sequence (SEQ ID NO : 274) derived from the coding sequence of : Figure 273.

Figure 275A-D shows a nucleotide sequence (SEQ ID NO : 275) of a native sequence PR083601 cDNA. Figure 275 is a clone designated herein as "DNA327580".

Figure 276 shows the amino acid sequence (SEQ ID NO : 276) derived from the coding sequence of : Figure 275A-D.

Figure 277A-B shows a nucleotide sequence (SEQ ID NO : 277) of a native sequence PR083602 cDNA. Figure 277 is a clone designated herein as "DNA327581".

Figure 278 shows the amino acid sequence (SEQ ID NO : 278) derived from the coding sequence of : Figure 277A-B.

Figure 279 shows a nucleotide sequence (SEQ ID NO : 279) of a native sequence PR02572 cDNA, w clone designated herein as "DNA83058".

Figure 280 shows the amino acid sequence (SEQ ID NO : 280) derived from the coding sequence of : Figure 279.

Figure 281 shows a nucleotide sequence (SEQ ID NO : 281) of a native sequence PR069486 cDNA, a clone designated herein as "DNA326896".

Figure 282 shows the amino acid sequence (SEQ ID NO : 282) derived from the coding sequence of Figure 281.

Figure 283 shows a nucleotide sequence (SEQ ID NO : 283) of a native sequence PR082442 cDNA, a clone designated herein as "DNA326000".

Figure 284 shows the amino acid sequence (SEQ ID NO : 284) derived from the coding sequence of Figure 283.

Figure 285 shows a nucleotide sequence (SEQ ID NO : 285) of a native sequence PR082432 cDNA, a clone designated herein as "DNA325988".

Figure 286 shows the amino acid sequence (SEQ ID NO : 286) derived from the coding sequence of Figure 285.

Figure 287 shows a nucleotide sequence (SEQ ID NO : 287) of a native sequence PRO1189 cDNA, a clone designated herein as "DNA58828".

Figure 288 shows the amino acid sequence (SEQ ID NO : 288) derived from the coding sequence of Figure 287.

Figure 289 shows a nucleotide sequence (SEQ ID NO : 289) of a native sequence PRO1189 cDNA, a clone designated herein as "DNA327192".

Figure 290 shows the amino acid sequence (SEQ ID NO : 290) derived from the coding sequence of Figure 289.

Figure 291A-G shows a nucleotide sequence (SEQ ID NO : 291) of a native sequence PR083603 cDI 291 is a clone designated herein as "DNA327582".

Figure 292 shows the amino acid sequence (SEQ ID NO : 292) derived from the coding sequence of Figure 291A-G.

Figure 293 shows a nucleotide sequence (SEQ ID NO : 293) of a native sequence PR049685 cDNA, a clone designated herein as "DNA254582".

Figure 294 shows the amino acid sequence (SEQ ID NO : 294) derived from the coding sequence of Figure 293.

Figure 295A-B shows a nucleotide sequence (SEQ ID NO : 295) of a native sequence PR083604 cDI 295 is a clone designated herein as "DNA327583".

Figure 296 shows the amino acid sequence (SEQ ID NO : 296) derived from the coding sequence of Figure 295A-B.

Figure 297 shows a nucleotide sequence (SEQ ID NO : 297) of a native sequence PR059082 cDNA, a clone designated herein as "DNA270719".

Figure 298 shows the amino acid sequence (SEQ ID NO : 298) derived from the coding sequence of Figure 297.

Figure 299 shows a nucleotide sequence (SEQ ID NO : 299) of a native sequence PR069559 cDNA, a clone designated herein as "DNA287289".

Figure 300 shows the amino acid sequence (SEQ ID NO : 300) derived from the coding sequence of Figure 299.

Figure 301 shows a nucleotide sequence (SEQ ID NO : 301) of a native sequence PR061125 cDNA, a clone designated herein as "DNA273060".

Figure 302 shows the amino acid sequence (SEQ ID NO : 302) derived from the coding sequence of Figure 301.

Figure 303 shows a nucleotide sequence (SEQ ID NO : 303) of a native sequence PR080649 cDNA, a clone designated herein as "DNA327584".

Figure 304 shows the amino acid sequence (SEQ ID NO : 304) derived from the coding sequence of Figure 303.

Figure 305 shows a nucleotide sequence (SEQ ID NO : 305) of a native sequence PRO12814 cDNA, a clone designated herein as "DNA150872".

Figure 306 shows the amino acid sequence (SEQ ID NO : 306) derived from the coding sequence of Figure 305.

Figure 307 shows a nucleotide sequence (SEQ ID NO : 307) of a native sequence PRO83605 cDNA, a clone designated herein as "DNA327585".

Figure 308 shows the amino acid sequence (SEQ ID NO : 308) derived from the coding sequence of Figure 307.

Figure 309A-B shows a nucleotide sequence (SEQ ID NO : 309) of a native sequence PR024100 cDI 309 is a clone designated herein as "DNA194837".

Figure 310 shows the amino acid sequence (SEQ ID NO : 310) derived from the coding sequence of Figure 309.

Figure 311 shows a nucleotide sequence (SEQ ID NO : 311) of a native sequence PRO82369 cDNA, a clone designated herein as "DNA325015".

Figure 312 shows the amino acid sequence (SEQ ID NO : 312) derived from the coding sequence of Figure 311.

Figure 313A-B shows a nucleotide sequence (SEQ ID NO : 313) of a native sequence PR02707 cDN is a clone designated herein as "DNA88229".

Figure 314 shows the amino acid sequence (SEQ ID NO : 314) derived from the coding sequence of Figure 313A-B.

Figure 315 shows a nucleotide sequence (SEQ ID NO : 315) of a native sequence PR02579 cDNA, a clone designated herein as "DNA327586".

Figure 316 shows the amino acid sequence (SEQ ID NO : 316) derived from the coding sequence of Figure 315.

Figure 317 shows a nucleotide sequence (SEQ ID NO : 317) of a native sequence PR033677 cDNA, a clone designated herein as "DNA210132".

Figure 318 shows the amino acid sequence (SEQ ID NO : 318) derived from the coding sequence of Figure 317.

Figure 319 shows a nucleotide sequence (SEQ ID NO : 319) of a native sequence PRO1720 cDNA, a clone designated herein as "DNA326840".

Figure 320 shows the amino acid sequence (SEQ ID NO : 320) derived from the coding sequence of Figure 319.

Figure 321 shows a nucleotide sequence (SEQ ID NO : 321) of a native sequence PR062607 cDNA, a clone designated herein as "DNA324049".

Figure 322 shows the amino acid sequence (SEQ ID NO : 322) derived from the coding sequence of Figure 321.

Figure 323A-B shows a nucleotide sequence (SEQ ID NO : 323) of a native sequence PRO12256 cDNA is a clone designated herein as "DNA150447".

Figure 324 shows the amino acid sequence (SEQ ID NO : 324) derived from the coding sequence of Figure 323A-B.

Figure 325 shows a nucleotide sequence (SEQ ID NO : 325) of a native sequence PR083606 cDNA, a clone designated herein as "DNA327587".

Figure 326 shows the amino acid sequence (SEQ ID NO : 326) derived from the coding sequence of Figure 325.



Figure 327 shows a nucleotide sequence (SEQ ID NO : 327) of a native sequence PRO59911 cDNA, a clone designated herein as "DNA271624".

Figure 328 shows the amino acid sequence (SEQ ID NO : 328) derived from the coding sequence of Figure 327.

Figure 329 shows a nucleotide sequence (SEQ ID NO : 329) of a native sequence PRO57964 cDNA, a clone designated herein as "DNA269548".

Figure 330 shows the amino acid sequence (SEQ ID NO : 330) derived from the coding sequence of Figure 329.

Figure 331 shows a nucleotide sequence (SEQ ID NO : 331) of a native sequence PRO83607 cDNA, a clone designated herein as "DNA327588".

Figure 332 shows the amino acid sequence (SEQ ID NO : 332) derived from the coding sequence of Figure 331.

Figure 333 shows a nucleotide sequence (SEQ ID NO : 333) of a native sequence PRO70806 cDNA, a clone designated herein as "DNA327589".

Figure 334 shows the amino acid sequence (SEQ ID NO : 334) derived from the coding sequence of Figure 333.

Figure 335 shows a nucleotide sequence (SEQ ID NO : 335) of a native sequence PRO2540 cDNA, a clone designated herein as "DNA76514".

Figure 336 shows the amino acid sequence (SEQ ID NO : 336) derived from the coding sequence of Figure 335.

Figure 337 shows a nucleotide sequence (SEQ ID NO : 337) of a native sequence PRO83608 cDNA, a clone designated herein as "DNA327590".

Figure 338 shows the amino acid sequence (SEQ ID NO : 338) derived from the coding sequence of Figure 337.

Figure 339A-E shows a nucleotide sequence (SEQ ID NO : 339) of a native sequence PRO83609 cDNA 339 is a clone designated herein as "DNA327591".

Figure 340 shows the amino acid sequence (SEQ ID NO : 340) derived from the coding sequence of Figure 339A-E.

Figure 341 shows a nucleotide sequence (SEQ ID NO : 341) of a native sequence PRO83610 cDNA, a clone designated herein as "DNA327592".

Figure 342 shows the amino acid sequence (SEQ ID NO : 342) derived from the coding sequence of Figure 341

Figure 343 shows a nucleotide sequence (SEQ ID NO : 343) of a native sequence PR062830 cDNA, a clone designated herein as "DNA287296".

Figure 344 shows the amino acid sequence (SEQ ID NO : 344) derived from the coding sequence of Figure 343.

Figure 345 shows a nucleotide sequence (SEQ ID NO : 345) of a native sequence PR059733 cDNA, a clone designated herein as "DNA327593".

Figure 346 shows the amino acid sequence (SEQ ID NO : 346) derived from the coding sequence of Figure 345.

Figure 347 shows a nucleotide sequence (SEQ ID NO : 347) of a native sequence PR081169 cDNA, a clone designated herein as "DNA324514".

Figure 348 shows the amino acid sequence (SEQ ID NO : 348) derived from the coding sequence of Figure 347.

Figure 349 shows a nucleotide sequence (SEQ ID NO : 349) of a native sequence PR02644 cDNA, a clone designated herein as "DNA88084".

Figure 350 shows the amino acid sequence (SEQ ID NO : 350) derived from the coding sequence of Figure 349.

Figure 351 shows a nucleotide sequence (SEQ ID NO : 351) of a native sequence PR037015 cDNA, a clone designated herein as "DNA287267".

Figure 352 shows the amino acid sequence (SEQ ID NO : 352) derived from the coding sequence of Figure 351.

Figure 353 shows a nucleotide sequence (SEQ ID NO : 353) of a native sequence PR061409 cDNA, a clone designated herein as "DNA273410".

Figure 354 shows the amino acid sequence (SEQ ID NO : 354) derived from the coding sequence of Figure 353.

Figure 355 shows a nucleotide sequence (SEQ ID NO : 355) of a native sequence PR04798 cDNA, a clone designated herein as "DNA103471".

Figure 356 shows the amino acid sequence (SEQ ID NO : 356) derived from the coding sequence of Figure 355.

Figure 357A-B shows a nucleotide sequence (SEQ ID NO : 357) of a native sequence PR02573 cDNA, is a clone designated herein as "DNA83061".

Figure 358 shows the amino acid sequence (SEQ ID NO : 358) derived from the coding sequence of Figure 357A-B.

Figure 359 shows a nucleotide sequence (SEQ ID NO : 359) of a native sequence PRO81936 cDNA, a clone designated herein as "DNA325404".

Figure 360 shows the amino acid sequence (SEQ ID NO : 360) derived from the coding sequence of Figure 359.

Figure 361 shows a nucleotide sequence (SEQ ID NO : 361) of a native sequence PRO80648 cDNA, a clone designated herein as "DNA323910".

Figure 362 shows the amino acid sequence (SEQ ID NO : 362) derived from the coding sequence of Figure 361.

Figure 363 shows a nucleotide sequence (SEQ ID NO : 363) of a native sequence PRO83611 cDNA, a clone designated herein as "DNA327594".

Figure 364 shows the amino acid sequence (SEQ ID NO : 364) derived from the coding sequence of Figure 363.

Figure 365 shows a nucleotide sequence (SEQ ID NO : 365) of a native sequence PRO83612 cDNA, a clone designated herein as "DNA327595".

Figure 366 shows the amino acid sequence (SEQ ID NO : 366) derived from the coding sequence of Figure 365.

Figure 367A-B shows a nucleotide sequence (SEQ ID NO : 367) of a native sequence PRO1920 cDNA 367 is a clone designated herein as "DNA327596".

Figure 368 shows the amino acid sequence (SEQ ID NO : 368) derived from the coding sequence of Figure 367A-B.

Figure 369A-B shows a nucleotide sequence (SEQ ID NO : 369) of a native sequence PRO83613 cDNA 369 is a clone designated herein as "DNA327597".

Figure 370 shows the amino acid sequence (SEQ ID NO : 370) derived from the coding sequence of Figure 369A-B.

Figure 371 shows a nucleotide sequence (SEQ ID NO : 371) of a native sequence PRO2831 cDNA, a clone designated herein as "DNA327598".

Figure 372 shows the amino acid sequence (SEQ ID NO : 372) derived from the coding sequence of Figure 371.

Figure 373A-B shows a nucleotide sequence (SEQ ID NO : 373) of a native sequence PRO83614 cDNA 373 is a clone designated herein as "DNA327599".

Figure 374 shows the amino acid sequence (SEQ ID NO : 374) derived from the coding sequence of Figure 373A-B.

Figure 375A-B shows a nucleotide sequence (SEQ ID NO : 375) of a native sequence PR038442 cDNA 375 is a clone designated herein as "DNA227979".

Figure 376 shows the amino acid sequence (SEQ ID NO : 376) derived from the coding sequence of Figure 375A-B.

Figure 377 shows a nucleotide sequence (SEQ ID NO : 377) of a native sequence PR059478 cDNA, a clone designated herein as "DNA271157".

Figure 378 shows the amino acid sequence (SEQ ID NO : 378) derived from the coding sequence of Figure 377.

Figure 379 shows a nucleotide sequence (SEQ ID NO : 379) of a native sequence PR060450 cDNA, a clone designated herein as "DNA272185".

Figure 380 shows the amino acid sequence (SEQ ID NO : 380) derived from the coding sequence of Figure 379.

Figure 381A-B shows a nucleotide sequence (SEQ ID NO : 381) of a native sequence PR04802 cDNA is a clone designated herein as "DNA103475".

Figure 382 shows the amino acid sequence (SEQ ID NO : 382) derived from the coding sequence of Figure 381.

Figure 383 shows a nucleotide sequence (SEQ ID NO : 383) of a native sequence PRO1192 cDNA, a clone designated herein as "DNA327600".

Figure 384 shows the amino acid sequence (SEQ ID NO : 384) derived from the coding sequence of Figure 383.

Figure 385 shows a nucleotide sequence (SEQ ID NO : 385) of a native sequence PR01192 cDNA, a clone designated herein as "DNA327601".

Figure 386 shows the amino acid sequence (SEQ ID NO : 386) derived from the coding sequence of Figure 385.

Figure 387 shows a nucleotide sequence (SEQ ID NO : 387) of a native sequence PR061296 cDNA, a clone designated herein as "DNA273286".

Figure 388 shows the amino acid sequence (SEQ ID NO : 388) derived from the coding sequence of : Figure 387.

Figure 389 shows a nucleotide sequence (SEQ ID NO : 389) of a native sequence PR045618 cDNA, a clone designated herein as "DNA327602".

Figure 390 shows the amino acid sequence (SEQ ID NO : 390) derived from the coding sequence of Figure 389.

Figure 391 shows a nucleotide sequence (SEQ ID NO : 391) of a native sequence PR058118 cDNA, a clone designated herein as "DNA327603".

Figure 392 shows the amino acid sequence (SEQ ID NO : 392) derived from the coding sequence of Figure 391.

Figure 393 shows a nucleotide sequence (SEQ ID NO : 393) of a native sequence PRO131 cDNA, a clone designated herein as "DNA53531".

Figure 394 shows the amino acid sequence (SEQ ID NO : 394) derived from the coding sequence of Figure 393. Figure 395 shows a nucleotide sequence (SEQ ID NO : 395) of a native sequence PR04 NO : 395 is a clone designated herein as "DNA327604".

Figure 396 shows the amino acid sequence (SEQ ID NO : 396) derived from the coding sequence of Figure 395.

Figure 397A-D shows a nucleotide sequence (SEQ ID NO : 397) of a native sequence PR083615 cDNA 397 is a clone designated herein as "DNA327605".

Figure 398A-B shows the amino acid sequence (SEQ ID NO : 398) derived from the coding sequence in Figure 397A-D.

Figure 399A-B shows a nucleotide sequence (SEQ ID NO : 399) of a native sequence PR036600 cDNA 399 is a clone designated herein as "DNA226137".

Figure 400 shows the amino acid sequence (SEQ ID NO : 400) derived from the coding sequence of Figure 399A-B.

Figure 401 shows a nucleotide sequence (SEQ ID NO : 401) of a native sequence PR057873 cDNA, a clone designated herein as "DNA327606".

Figure 402 shows the amino acid sequence (SEQ ID NO : 402) derived from the coding sequence of Figure 401.

Figure 403 shows a nucleotide sequence (SEQ ID NO : 403) of a native sequence PR083616 cDNA, a clone designated herein as "DNA327607".

Figure 404 shows the amino acid sequence (SEQ ID NO : 404) derived from the coding sequence of Figure 403.

Figure 405 shows a nucleotide sequence (SEQ ID NO : 405) of a native sequence PR062740 cDNA.

a clone designated herein as "DNA275012".

Figure 406 shows the amino acid sequence (SEQ ID NO : 406) derived from the coding sequence of Figure 405.

Figure 407 shows a nucleotide sequence (SEQ ID NO : 407) of a native sequence PRO83617 cDNA, a clone designated herein as "DNA327608".

Figure 408 shows the amino acid sequence (SEQ ID NO : 408) derived from the coding sequence of Figure 407.

Figure 409 shows a nucleotide sequence (SEQ ID NO : 409) of a native sequence PR036596 cDNA, a clone designated herein as "DNA226133".

Figure 410 shows the amino acid sequence (SEQ ID NO : 410) derived from the coding sequence of Figure 409.

Figure 411 shows a nucleotide sequence (SEQ ID NO : 411) of a native sequence PR03629 cDNA, a clone designated herein as "DNA326089".

Figure 412 shows the amino acid sequence (SEQ ID NO : 412) derived from the coding sequence of Figure 411.

Figure 413 shows a nucleotide sequence (SEQ ID NO : 413) of a native sequence PR057934 cDNA, a clone designated herein as "DNA269518".

Figure 414 shows the amino acid sequence (SEQ ID NO : 414) derived from the coding sequence of Figure 413.

Figure 415 shows a nucleotide sequence (SEQ ID NO : 415) of a native sequence PR083618 cDNA, a clone designated herein as "DNA327609".

Figure 416 shows the amino acid sequence (SEQ ID NO : 416) derived from the coding sequence of Figure 415.

Figure 417 shows a nucleotide sequence (SEQ ID NO : 417) of a native sequence PR070595 cDNA, a clone designated herein as "DNA290319".

Figure 418 shows the amino acid sequence (SEQ ID NO : 418) derived from the coding sequence of Figure 417.

Figure 419 shows a nucleotide sequence (SEQ ID NO : 419) of a native sequence PR060781 cDNA, a clone designated herein as "DNA272655".

Figure 420 shows the amino acid sequence (SEQ ID NO : 420) derived from the coding sequence of Figure 419.

Figure 421 shows a nucleotide sequence (SEQ ID NO : 421) of a native sequence PRO12186 cDNA, a clone designated herein as "DNA151798".

Figure 422 shows the amino acid sequence (SEQ ID NO : 422) derived from the coding sequence of Figure 421.

Figure 423 shows a nucleotide sequence (SEQ ID NO : 423) of a native sequence PR037977 cDNA, a clone designated herein as "DNA227514".

Figure 424 shows the amino acid sequence (SEQ ID NO : 424) derived from the coding sequence of Figure 423.

Figure 425 shows a nucleotide sequence (SEQ ID NO : 425) of a native sequence PR083619 cDNA, a clone designated herein as "DNA327610".

Figure 426 shows the amino acid sequence (SEQ ID NO : 426) derived from the coding sequence of Figure 425.

Figure 427A-B shows a nucleotide sequence (SEQ ID NO : 427) of a native sequence PR083620 cDNA 427 is a clone designated herein as "DNA327611".

Figure 428 shows the amino acid sequence (SEQ ID NO : 428) derived from the coding sequence of Figure 427A-B.

Figure 429 shows a nucleotide sequence (SEQ ID NO : 429) of a native sequence PR083621 cDNA, a clone designated herein as "DNA327612".

Figure 430 shows the amino acid sequence (SEQ ID NO : 430) derived from the coding sequence of Figure 429.

Figure 431 shows a nucleotide sequence (SEQ ID NO : 431) of a native sequence PRO82689 cDNA, a clone designated herein as "DNA326287".

Figure 432 shows the amino acid sequence (SEQ ID NO : 432) derived from the coding sequence of Figure 431.

Figure 433 shows a nucleotide sequence (SEQ ID NO : 433) of a native sequence PR083622 cDNA, a clone designated herein as "DNA327613".

Figure 434 shows the amino acid sequence (SEQ ID NO : 434) derived from the coding sequence of Figure 433.

Figure 435 shows a nucleotide sequence (SEQ ID NO : 435) of a native sequence PRO11 cDNA, which clone designated herein as "DNA327614".

Figure 436 shows the amino acid sequence (SEQ ID NO : 436) derived from the coding sequence of

Figure 435.

Figure 437A-B shows a nucleotide sequence (SEQ ID NO : 437) of a native sequence PRO83623 cD 437 is a clone designated herein as "DNA327615".

Figure 438 shows the amino acid sequence (SEQ ID NO : 438) derived from the coding sequence of Figure 437A-B.

Figure 439 shows a nucleotide sequence (SEQ ID NO : 439) of a native sequence PRO83624 cDNA, a clone designated herein as "DNA327616".

Figure 440 shows the amino acid sequence (SEQ ID NO : 440) derived from the coding sequence of Figure 439.

Figure 441 shows a nucleotide sequence (SEQ ID NO : 441) of a native sequence PRO36219 cDNA, a clone designated herein as "DNA225756".

Figure 442 shows the amino acid sequence (SEQ ID NO : 442) derived from the coding sequence of Figure 441.

Figure 443 shows a nucleotide sequence (SEQ ID NO : 443) of a native sequence PR04793 cDNA, a clone designated herein as "DNA325800".

Figure 444 shows the amino acid sequence (SEQ ID NO : 444) derived from the coding sequence of Figure 443.

Figure 445 shows a nucleotide sequence (SEQ ID NO : 445) of a native sequence PRO83625 cDNA, a clone designated herein as "DNA327617".

Figure 446 shows the amino acid sequence (SEQ ID NO : 446) derived from the coding sequence of Figure 445.

Figure 447 shows a nucleotide sequence (SEQ ID NO : 447) of a native sequence PR049481 cDNA, a clone designated herein as "DNA254370".

Figure 448 shows the amino acid sequence (SEQ ID NO : 448) derived from the coding sequence of Figure 447.

Figure 449A-B shows a nucleotide sequence (SEQ ID NO : 449) of a native sequence PR083626 cD 449 is a clone designated herein as "DNA327618".

Figure 450 shows the amino acid sequence (SEQ ID NO : 450) derived from the coding sequence of Figure 449A-B.

Figure 451 shows a nucleotide sequence (SEQ ID NO : 451) of a native sequence PR083627 cDNA, a clone designated herein as "DNA327619".



Figure 452 shows the amino acid sequence (SEQ ID NO : 452) derived from the coding sequence of Figure 451.

Figure 453 shows a nucleotide sequence (SEQ ID NO : 453) of a native sequence PRO12754 cDNA, a clone designated herein as "DNA151910".

Figure 454 shows the amino acid sequence (SEQ ID NO : 454) derived from the coding sequence of Figure 453.

Figure 455A-C shows a nucleotide sequence (SEQ ID NO : 455) of a native sequence PR036778 cDNA, 455 is a clone designated herein as "DNA226315".

Figure 456 shows the amino acid sequence (SEQ ID NO : 456) derived from the coding sequence of Figure 455.

Figure 457 shows a nucleotide sequence (SEQ ID NO : 457) of a native sequence PR04633 cDNA, a clone designated herein as "DNA327620".

Figure 458 shows the amino acid sequence (SEQ ID NO : 458) derived from the coding sequence of Figure 457.

Figure 459 shows a nucleotide sequence (SEQ ID NO : 459) of a native sequence PRO83628 cDNA, a clone designated herein as "DNA327621".

Figure 460 shows the amino acid sequence (SEQ ID NO : 460) derived from the coding sequence of Figure 459.

Figure 461 shows a nucleotide sequence (SEQ ID NO : 461) of a native sequence PRO83472 cDNA, a clone designated herein as "DNA327196".

Figure 462 shows the amino acid sequence (SEQ ID NO : 462) derived from the coding sequence of Figure 461.

Figure 463 shows a nucleotide sequence (SEQ ID NO : 463) of a native sequence PRO83629 cDNA, a clone designated herein as "DNA327622".

Figure 464 shows the amino acid sequence (SEQ ID NO : 464) derived from the coding sequence of Figure 463.

Figure 465A-B shows a nucleotide sequence (SEQ ID NO : 465) of a native sequence PRO12278 cDNA, 465 is a clone designated herein as "DNA150475".

Figure 466 shows the amino acid sequence (SEQ ID NO : 466) derived from the coding sequence of Figure 465A-B.

Figure 466 shows a nucleotide sequence (SEQ ID NO : 466) of a native sequence PR024089 cDNA

a clone designated herein as "DNA327623".

Figure 467 shows the amino acid sequence (SEQ ID NO : 467) derived from the coding sequence of Figure 466.

Figure 469 shows a nucleotide sequence (SEQ ID NO : 469) of a native sequence PR060979 cDNA, a clone designated herein as "DNA272889".

Figure 470 shows the amino acid sequence (SEQ ID NO : 470) derived from the coding sequence of Figure 469.

Figure 471 shows a nucleotide sequence (SEQ ID NO : 471) of a native sequence PR083630 cDNA, a clone designated herein as "DNA327624".

Figure 472 shows the amino acid sequence (SEQ ID NO : 472) derived from the coding sequence of Figure 471.

Figure 473 shows a nucleotide sequence (SEQ ID NO : 473) of a native sequence PR011985 cDNA, a clone designated herein as "DNA151689".

Figure 474 shows the amino acid sequence (SEQ ID NO : 474) derived from the coding sequence of Figure 473.

Figure 475 shows a nucleotide sequence (SEQ ID NO : 475) of a native sequence PR060900 cDNA, a clone designated herein as "DNA272795".

Figure 476 shows the amino acid sequence (SEQ ID NO : 476) derived from the coding sequence of Figure 475.

Figure 477 shows a nucleotide sequence (SEQ ID NO : 477) of a native sequence PR036124 cDNA, a clone designated herein as "DNA225661".

Figure 478 shows the amino acid sequence (SEQ ID NO : 478) derived from the coding sequence of Figure 477.

Figure 479 shows a nucleotide sequence (SEQ ID NO : 479) of a native sequence PR061634 cDNA, a clone designated herein as "DNA273666".

Figure 480 shows the amino acid sequence (SEQ ID NO : 480) derived from the coding sequence of Figure 479.

Figure 481 shows a nucleotide sequence (SEQ ID NO : 481) of a native sequence PR037065 cDNA, a clone designated herein as "DNA226602".

Figure 482 shows the amino acid sequence (SEQ ID NO : 482) derived from the coding sequence of Figure 481.

Figure 483 shows a nucleotide sequence (SEQ ID NO : 483) of a native sequence PR025138 cDNA, a clone designated herein as "DNA327625".

Figure 484 shows the amino acid sequence (SEQ ID NO : 484) derived from the coding sequence of Figure 483.

Figure 485 shows a nucleotide sequence (SEQ ID NO : 485) of a native sequence PR037779 cDNA, a clone designated herein as "DNA327626".

Figure 486 shows the amino acid sequence (SEQ ID NO : 486) derived from the coding sequence of Figure 485.

Figure 487 shows a nucleotide sequence (SEQ ID NO : 487) of a native sequence PR069656 cDNA, a clone designated herein as "DNA287399".

Figure 488 shows the amino acid sequence (SEQ ID NO : 488) derived from the coding sequence of Figure 487.

Figure 489A-B shows a nucleotide sequence (SEQ ID NO : 489) of a native sequence PR083631 cDI 489 is a clone designated herein as "DNA327627".

Figure 490 shows the amino acid sequence (SEQ ID NO : 490) derived from the coding sequence of Figure 489A-B.

Figure 491 shows a nucleotide sequence (SEQ ID NO : 491) of a native sequence PR083632 cDNA, a clone designated herein as "DNA327628".

Figure 492 shows the amino acid sequence (SEQ ID NO : 492) derived from the coding sequence of Figure 491.

Figure 493 shows a nucleotide sequence (SEQ ID NO : 493) of a native sequence PRO83633 cDNA, a clone designated herein as "DNA327629".

Figure 494 shows the amino acid sequence (SEQ ID NO : 494) derived from the coding sequence of Figure 493.

Figure 495A-B shows a nucleotide sequence (SEQ ID NO : 495) of a native sequence PR036043 cDI 495 is a clone designated herein as "DNA225580".

Figure 496 shows the amino acid sequence (SEQ ID NO : 496) derived from the coding sequence of Figure 495A-B.

Figure 497 shows a nucleotide sequence (SEQ ID NO : 497) of a native sequence PR060569 cDNA, a clone designated herein as "DNA272312".

Figure 498 shows the amino acid sequence (SEQ ID NO : 498) derived from the coding sequence of

Figure 497.

Figure 499 shows a nucleotide sequence (SEQ ID NO : 499) of a native sequence PR038724 cDNA, a clone designated herein as "DNA327630".

Figure 500 shows the amino acid sequence (SEQ ID NO : 500) derived from the coding sequence of Figure 499.

Figure 501 shows a nucleotide sequence (SEQ ID NO : 501) of a native sequence PR083634 cDNA, a clone designated herein as "DNA327631".

Figure 502 shows the amino acid sequence (SEQ ID NO : 502) derived from the coding sequence of Figure 501.

Figure 503 shows a nucleotide sequence (SEQ ID NO : 503) of a native sequence PR083635 cDNA, a clone designated herein as "DNA327632".

Figure 504 shows the amino acid sequence (SEQ ID NO : 504) derived from the coding sequence of Figure 503.

Figure 505 shows a nucleotide sequence (SEQ ID NO : 505) of a native sequence PR082726 cDNA, a clone designated herein as "DNA326328".

Figure 506 shows the amino acid sequence (SEQ ID NO : 506) derived from the coding sequence of Figure 505.

Figure 507 shows a nucleotide sequence (SEQ ID NO : 507) of a native sequence PR02870 cDNA, a clone designated herein as "DNA327633".

Figure 508 shows the amino acid sequence (SEQ ID NO : 508) derived from the coding sequence of Figure 507.

Figure 509 shows a nucleotide sequence (SEQ ID NO : 509) of a native sequence PR02885 cDNA, a clone designated herein as "DNA88654".

Figure 510 shows the amino acid sequence (SEQ ID NO : 510) derived from the coding sequence of Figure 509.

Figure 511 shows a nucleotide sequence (SEQ ID NO : 511) of a native sequence PR083636 cDNA, a clone designated herein as "DNA327634".

Figure 512 shows the amino acid sequence (SEQ ID NO : 512) derived from the coding sequence of Figure 511.

Figure 513 shows a nucleotide sequence (SEQ ID NO : 513) of a native sequence PR021708 cDNA, a clone designated herein as "DNA188333".

Figure 514 shows the amino acid sequence (SEQ ID NO : 514) derived from the coding sequence of Figure 513.

Figure 515 shows a nucleotide sequence (SEQ ID NO : 515) of a native sequence PR021825 cDNA, a clone designated herein as "DNA188269".

Figure 516 shows the amino acid sequence (SEQ ID NO : 516) derived from the coding sequence of Figure 515.

Figure 517A-B shows a nucleotide sequence (SEQ ID NO : 517) of a native sequence PR036946 cDNA, a clone designated herein as "DNA226483".

Figure 518 shows the amino acid sequence (SEQ ID NO : 518) derived from the coding sequence of Figure 517A-B.

Figure 519 shows a nucleotide sequence (SEQ ID NO : 519) of a native sequence PR049203 cDNA, a clone designated herein as "DNA253798".

Figure 520 shows the amino acid sequence (SEQ ID NO : 520) derived from the coding sequence of Figure 520.

Figure 521 shows a nucleotide sequence (SEQ ID NO : 521) of a native sequence PRO59526 cDNA, a clone designated herein as "DNA27121".

Figure 522 shows the amino acid sequence (SEQ ID NO : 522) derived from the coding sequence of Figure 521.

Figure 523 shows a nucleotide sequence (SEQ ID NO : 523) of a native sequence PR059946 cDNA, a clone designated herein as "DNA271660".

Figure 524 shows the amino acid sequence (SEQ ID NO : 524) derived from the coding sequence of Figure 523.

Figure 525 shows a nucleotide sequence (SEQ ID NO : 525) of a native sequence PRO83637 cDNA, a clone designated herein as "DNA327635".

Figure 526 shows the amino acid sequence (SEQ ID NO : 526) derived from the coding sequence of Figure 525.

Figure 527 shows a nucleotide sequence (SEQ ID NO : 527) of a native sequence PR02703 cDNA, a clone designated herein as "DNA88215".

Figure 528 shows the amino acid sequence (SEQ ID NO : 528) derived from the coding sequence of Figure 527.

Figure 529 shows a nucleotide sequence (SEQ ID NO : 529) of a native sequence PR052392 cDNA

a clone designated herein as "DNA257852".

Figure 530 shows the amino acid sequence (SEQ ID NO : 530) derived from the coding sequence of Figure 529.

Figure 531 shows a nucleotide sequence (SEQ ID NO : 531) of a native sequence PR083638 cDNA, a clone designated herein as "DNA327636".

Figure 532 shows the amino acid sequence (SEQ ID NO : 532) derived from the coding sequence of Figure 531.

Figure 533 shows a nucleotide sequence (SEQ ID NO : 533) of a native sequence PR02552 cDNA, a clone designated herein as "DNA327637".

Figure 534 shows the amino acid sequence (SEQ ID NO : 534) derived from the coding sequence of Figure 533.

Figure 535 shows a nucleotide sequence (SEQ ID NO : 535) of a native sequence PR083639 cDNA, a clone designated herein as "DNA327638".

Figure 536 shows the amino acid sequence (SEQ ID NO : 536) derived from the coding sequence of Figure 535.

Figure 537 shows a nucleotide sequence (SEQ ID NO : 537) of a native sequence PR069600 cDNA, a clone designated herein as "DNA287337".

Figure 538 shows the amino acid sequence (SEQ ID NO : 538) derived from the coding sequence of Figure 537.

Figure 539 shows a nucleotide sequence (SEQ ID NO : 539) of a native sequence PR036650 cDNA, a clone designated herein as "DNA226187".

Figure 540 shows the amino acid sequence (SEQ ID NO : 540) derived from the coding sequence of Figure 539.

Figure 541 shows a nucleotide sequence (SEQ ID NO : 541) of a native sequence PR021885 cDNA, a clone designated herein as "DNA188355".

Figure 542 shows the amino acid sequence (SEQ ID NO : 542) derived from the coding sequence of Figure 541.

Figure 543 shows a nucleotide sequence (SEQ ID NO : 543) of a native sequence PR069503 cDNA, a clone designated herein as "DNA287224".

Figure 544 shows the amino acid sequence (SEQ ID NO : 544) derived from the coding sequence of Figure 543.

Figure 545 shows a nucleotide sequence (SEQ ID NO : 545) of a native sequence PRO83640 cDNA, a clone designated herein as "DNA327639".

Figure 546 shows the amino acid sequence (SEQ ID NO : 546) derived from the coding sequence of Figure 545.

Figure 547 shows a nucleotide sequence (SEQ ID NO : 547) of a native sequence PRO83641 cDNA, a clone designated herein as "DNA327640".

Figure 548 shows the amino acid sequence (SEQ ID NO : 548) derived from the coding sequence of Figure 547.

Figure 549 shows a nucleotide sequence (SEQ ID NO : 549) of a native sequence PRO83642 cDNA, a clone designated herein as "DNA327641".

Figure 550 shows the amino acid sequence (SEQ ID NO : 550) derived from the coding sequence of Figure 549.

Figure 551 shows a nucleotide sequence (SEQ ID NO : 551) of a native sequence PRO83643 cDNA, a clone designated herein as "DNA327642".

Figure 552 shows the amino acid sequence (SEQ ID NO : 552) derived from the coding sequence of Figure 551.

Figure 553 shows a nucleotide sequence (SEQ ID NO : 553) of a native sequence PRO51301 cDNA, a clone designated herein as "DNA256257".

Figure 554 shows the amino acid sequence (SEQ ID NO : 554) derived from the coding sequence of Figure 553.

Figure 555A-B shows a nucleotide sequence (SEQ ID NO : 555) of a native sequence PRO83644 cDNA, a clone designated herein as "DNA327643".

Figure 556 shows the amino acid sequence (SEQ ID NO : 556) derived from the coding sequence of Figure 555A-B.

Figure 557 shows a nucleotide sequence (SEQ ID NO : 557) of a native sequence PRO2267 cDNA, a clone designated herein as "DNA88281".

Figure 558 shows the amino acid sequence (SEQ ID NO : 558) derived from the coding sequence of Figure 557.

Figure 559 shows a nucleotide sequence (SEQ ID NO : 559) of a native sequence PRO81000 cDNA, a clone designated herein as "DNA324324".

Figure 560 shows the amino acid sequence (SEQ ID NO : 560) derived from the coding sequence of

Figure 559.

Figure 561 shows a nucleotide sequence (SEQ ID NO : 561) of a native sequence PR069582 cDNA, a clone designated herein as "DNA287317".

Figure 562 shows the amino acid sequence (SEQ ID NO : 562) derived from the coding sequence of Figure 561.

Figure 563 shows a nucleotide sequence (SEQ ID NO : 563) of a native sequence PR083645 cDNA, a clone designated herein as "DNA327644".

Figure 564 shows the amino acid sequence (SEQ ID NO : 564) derived from the coding sequence of Figure 563.

Figure 565 shows a nucleotide sequence (SEQ ID NO : 565) of a native sequence PR02715 cDNA, a clone designated herein as "DNA88248".

Figure 566 shows the amino acid sequence (SEQ ID NO : 566) derived from the coding sequence of Figure 565.

Figure 567 shows a nucleotide sequence (SEQ ID NO : 567) of a native sequence PR083646 cDNA, a clone designated herein as "DNA327645".

Figure 568 shows the amino acid sequence (SEQ ID NO : 568) derived from the coding sequence of Figure 567.

Figure 569 shows a nucleotide sequence (SEQ ID NO : 569) of a native sequence PR083647 cDNA, a clone designated herein as "DNA327646".

Figure 570 shows the amino acid sequence (SEQ ID NO : 570) derived from the coding sequence of Figure 569.

Figure 571A-B shows a nucleotide sequence (SEQ ID NO : 571) of a native sequence PR012449 cDNA, a clone designated herein as "DNA226859".

Figure 572 shows the amino acid sequence (SEQ ID NO : 572) derived from the coding sequence of Figure 571A-B.

Figure 573 shows a nucleotide sequence (SEQ ID NO : 573) of a native sequence PR036372 cDNA, a clone designated herein as "DNA225909".

Figure 574 shows the amino acid sequence (SEQ ID NO : 574) derived from the coding sequence of Figure 573.

Figure 575 shows a nucleotide sequence (SEQ ID NO : 575) of a native sequence PR02447 cDNA, a clone designated herein as "DNA327647".



Figure 576 shows the amino acid sequence (SEQ ID NO : 576) derived from the coding sequence of Figure 575.

Figure 577 shows a nucleotide sequence (SEQ ID NO : 577) of a native sequence PR083648 cDNA, a clone designated herein as "DNA327648".

Figure 578 shows the amino acid sequence (SEQ ID NO : 578) derived from the coding sequence of Figure 577.

Figure 579A-B shows a nucleotide sequence (SEQ ID NO : 579) of a native sequence PR04673 cDN, is a clone designated herein as "DNA327649".

Figure 580 shows the amino acid sequence (SEQ ID NO : 580) derived from the coding sequence of Figure 579A-B.

Figure 581 shows a nucleotide sequence (SEQ ID NO : 581) of a native sequence PRO12489 cDNA, a clone designated herein as "DNA150830".

Figure 582 shows the amino acid sequence (SEQ ID NO : 582) derived from the coding sequence of Figure 581.

Figure 583 shows a nucleotide sequence (SEQ ID NO : 583) of a native sequence PR036008 cDNA, a clone designated herein as "DNA327650".

Figure 584 shows the amino acid sequence (SEQ ID NO : 584) derived from the coding sequence of Figure 583.

Figure 585 shows a nucleotide sequence (SEQ ID NO : 585) of a native sequence PR083649 cDNA, a clone designated herein as "DNA327651".

Figure 586 shows the amino acid sequence (SEQ ID NO : 586) derived from the coding sequence of Figure 585.

Figure 587 shows a nucleotide sequence (SEQ ID NO : 587) of a native sequence PR070423 cDNA, a clone designated herein as "DNA290279".

Figure 588 shows the amino acid sequence (SEQ ID NO : 588) derived from the coding sequence of Figure 587.

Figure 589A-B shows a nucleotide sequence (SEQ ID NO : 589) of a native sequence PR050365 cDI 589 is a clone designated herein as "DNA255292".

Figure 590 shows the amino acid sequence (SEQ ID NO : 590) derived from the coding sequence of Figure 589A-B.

Figure 591 shows a nucleotide sequence (SEQ ID NO : 591) of a native sequence PR058149 cDNA

a clone designated herein as "DNA269740".

Figure 592 shows the amino acid sequence (SEQ ID NO : 592) derived from the coding sequence of Figure 591.

Figure 593A-B shows a nucleotide sequence (SEQ ID NO : 593) of a native sequence PR02628 cDN is a clone designated herein as "DNA327652".

Figure 594 shows the amino acid sequence (SEQ ID NO : 594) derived from the coding sequence of Figure 593A-B.

Figure 595 shows a nucleotide sequence (SEQ ID NO : 595) of a native sequence PR049580 cDNA, a clone designated herein as "DNA254472".

Figure 596 shows the amino acid sequence (SEQ ID NO : 596) derived from the coding sequence of Figure 595.

Figure 597 shows a nucleotide sequence (SEQ ID NO : 597) of a native sequence PR059596 cDNA, a clone designated herein as "DNA327653".

Figure 598 shows the amino acid sequence (SEQ ID NO : 598) derived from the coding sequence of Figure 597.

Figure 599 shows a nucleotide sequence (SEQ ID NO : 599) of a native sequence PR059210 cDNA, a clone designated herein as "DNA270875".

Figure 600 shows the amino acid sequence (SEQ ID NO : 600) derived from the coding sequence of Figure 599.

Figure 601A-B shows a nucleotide sequence (SEQ ID NO : 601) of a native sequence PR070395 cDI 601 is a clone designated herein as "DNA290265".

Figure 602 shows the amino acid sequence (SEQ ID NO : 602) derived from the coding sequence of Figure 601A-B.

Figure 603 shows a nucleotide sequence (SEQ ID NO : 603) of a native sequence PR058792 cDNA, a clone designated herein as "DNA270411".

Figure 604 shows the amino acid sequence (SEQ ID NO : 604) derived from the coding sequence of Figure 603.

Figure 605 shows a nucleotide sequence (SEQ ID NO : 605) of a native sequence PR083650 cDNA, a clone designated herein as "DNA327654".

Figure 606 shows the amino acid sequence (SEQ ID NO : 606) derived from the coding sequence of Figure 605.

Figure 607 shows a nucleotide sequence (SEQ ID NO : 607) of a native sequence PR0322 cDNA, w  
clone designated herein as "DNA327655".

Figure 608 shows the amino acid sequence (SEQ ID NO : 608) derived from the coding sequence of  
Figure 607.

Figure 609 shows a nucleotide sequence (SEQ ID NO : 609) of a native sequence PR069572 cDNA,  
a clone designated herein as "DNA287306".

Figure 610 shows the amino acid sequence (SEQ ID NO : 610) derived from the coding sequence of  
Figure 609.

Figure 611 shows a nucleotide sequence (SEQ ID NO : 611) of a native sequence PR036117 cDNA,  
a clone designated herein as "DNA327656".

Figure 612 shows the amino acid sequence (SEQ ID NO : 612) derived from the coding sequence of  
Figure 611.

Figure 613 shows a nucleotide sequence (SEQ ID NO : 613) of a native sequence PR059399 cDNA,  
a clone designated herein as "DNA271075".

Figure 614 shows the amino acid sequence (SEQ ID NO : 614) derived from the coding sequence of  
Figure 613.

Figure 615A-B shows a nucleotide sequence (SEQ ID NO : 615) of a native sequence PR038147 cD  
615 is a clone designated herein as "DNA327657".

Figure 616 shows the amino acid sequence (SEQ ID NO : 616) derived from the coding sequence of  
Figure 615.

Figure 617 shows a nucleotide sequence (SEQ ID NO : 617) of a native sequence PRO83651 cDNA  
a clone designated herein as "DNA327658".

Figure 618 shows the amino acid sequence (SEQ ID NO : 618) derived from the coding sequence of  
Figure 617.

Figure 619 shows a nucleotide sequence (SEQ ID NO : 619) of a native sequence PR036302 cDNA,  
a clone designated herein as "DNA225839".

Figure 620 shows the amino acid sequence (SEQ ID NO : 620) derived from the coding sequence of  
Figure 619.

Figure 621 shows a nucleotide sequence (SEQ ID NO : 621) of a native sequence PR070443 cDNA,  
a clone designated herein as "DNA327659".

Figure 622 shows the amino acid sequence (SEQ ID NO : 622) derived from the coding sequence of

Figure 621.

Figure 623 shows a nucleotide sequence (SEQ ID NO : 623) of a native sequence PR02063 cDNA, a clone designated herein as "DNA83055".

Figure 624 shows the amino acid sequence (SEQ ID NO : 624) derived from the coding sequence of Figure 623.

Figure 625 shows a nucleotide sequence (SEQ ID NO : 625) of a native sequence PR0327 cDNA, a clone designated herein as "DNA327660".

Figure 626 shows the amino acid sequence (SEQ ID NO : 626) derived from the coding sequence of Figure 625.

Figure 627 shows a nucleotide sequence (SEQ ID NO : 627) of a native sequence PR083652 cDNA, a clone designated herein as "DNA327661".

Figure 628 shows the amino acid sequence (SEQ ID NO : 628) derived from the coding sequence of Figure 627.

Figure 629 shows a nucleotide sequence (SEQ ID NO : 629) of a native sequence PR036992 cDNA, a clone designated herein as "DNA299878".

Figure 630 shows the amino acid sequence (SEQ ID NO : 630) derived from the coding sequence of Figure 629.

Figure 631 shows a nucleotide sequence (SEQ ID NO : 631) of a native sequence PR02018 cDNA, a clone designated herein as "DNA75863".

Figure 632 shows the amino acid sequence (SEQ ID NO : 632) derived from the coding sequence of Figure 631.

Figure 633 shows a nucleotide sequence (SEQ ID NO : 633) of a native sequence PR038396 cDNA, a clone designated herein as "DNA227933".

Figure 634 shows the amino acid sequence (SEQ ID NO : 634) derived from the coding sequence of Figure 633.

Figure 635A-B shows a nucleotide sequence (SEQ ID NO : 635) of a native sequence cDNA, where designated herein as "DNA327662".

Figure 636 shows a nucleotide sequence (SEQ ID NO : 636) of a native sequence PR037683 cDNA, a clone designated herein as "DNA227220".

Figure 637 shows the amino acid sequence (SEQ ID NO : 637) derived from the coding sequence of Figure 636.

Figure 638 shows a nucleotide sequence (SEQ ID NO : 638) of a native sequence PR035062 cDNA, a clone designated herein as "DNA213596".

Figure 639 shows the amino acid sequence (SEQ ID NO : 639) derived from the coding sequence of Figure 638.

Figure 640 shows a nucleotide sequence (SEQ ID NO : 640) of a native sequence PR081618 cDNA, a clone designated herein as "DNA325029".

Figure 641 shows the amino acid sequence (SEQ ID NO : 641) derived from the coding sequence of Figure 640.

Figure 642 shows a nucleotide sequence (SEQ ID NO : 642) of a native sequence PR083654 cDNA, a clone designated herein as "DNA327663".

Figure 643 shows the amino acid sequence (SEQ ID NO : 643) derived from the coding sequence of Figure 642.

Figure 644 shows a nucleotide sequence (SEQ ID NO : 644) of a native sequence PR02722 cDNA, a clone designated herein as "DNA327664".

Figure 645 shows the amino acid sequence (SEQ ID NO : 645) derived from the coding sequence of Figure 644.

Figure 646 shows a nucleotide sequence (SEQ ID NO : 646) of a native sequence PR038104 cDNA, a clone designated herein as "DNA227641".

Figure 647 shows the amino acid sequence (SEQ ID NO : 647) derived from the coding sequence of Figure 646.

Figure 648 shows a nucleotide sequence (SEQ ID NO : 648) of a native sequence PRO83655 cDNA, a clone designated herein as "DNA327665".

Figure 649 shows the amino acid sequence (SEQ ID NO : 649) derived from the coding sequence of Figure 650.

Figure 650 shows a nucleotide sequence (SEQ ID NO : 650) of a native sequence PRO83656 cDNA, a clone designated herein as "DNA327666".

Figure 651 shows the amino acid sequence (SEQ ID NO : 651) derived from the coding sequence of Figure 650.

Figure 652 shows a nucleotide sequence (SEQ ID NO : 652) of a native sequence PRO83135 cDNA, a clone designated herein as "DNA327667".

Figure 653 shows the amino acid sequence (SEQ ID NO : 653) derived from the coding sequence of

Figure 652.

Figure 654 shows a nucleotide sequence (SEQ ID NO : 654) of a native sequence PRO83141 cDNA, a clone designated herein as "DNA327668".

Figure 655 shows the amino acid sequence (SEQ ID NO : 655) derived from the coding sequence of Figure 654.

Figure 656 shows a nucleotide sequence (SEQ ID NO : 656) of a native sequence PR083657 cDNA, a clone designated herein as "DNA327669".

Figure 657 shows the amino acid sequence (SEQ ID NO : 657) derived from the coding sequence of Figure 656.

Figure 658 shows a nucleotide sequence (SEQ ID NO : 658) of a native sequence PRO1288 cDNA, a clone designated herein as "DNA327670".

Figure 659 shows the amino acid sequence (SEQ ID NO : 659) derived from the coding sequence of Figure 658.

Figure 660 shows a nucleotide sequence (SEQ ID NO : 660) of a native sequence PRO83658 cDNA, a clone designated herein as "DNA327671".

Figure 661 shows the amino acid sequence (SEQ ID NO : 661) derived from the coding sequence of Figure 660.

Figure 662 shows a nucleotide sequence (SEQ ID NO : 662) of a native sequence PR02200 cDNA, a clone designated herein as "DNA88155".

Figure 663 shows the amino acid sequence (SEQ ID NO : 663) derived from the coding sequence of Figure 662.

Figure 664 shows a nucleotide sequence (SEQ ID NO : 664) of a native sequence PR058669 cDNA, a clone designated herein as "DNA270281".

Figure 665 shows the amino acid sequence (SEQ ID NO : 665) derived from the coding sequence of Figure 664.

Figure 666 shows a nucleotide sequence (SEQ ID NO : 666) of a native sequence PR083659 cDNA, a clone designated herein as "DNA327672".

Figure 667 shows the amino acid sequence (SEQ ID NO : 667) derived from the coding sequence of Figure 666.

Figure 668 shows a nucleotide sequence (SEQ ID NO : 668) of a native sequence PR021820 cDNA, a clone designated herein as "DNA188289".

Figure 669 shows the amino acid sequence (SEQ ID NO : 669) derived from the coding sequence of Figure 668.

Figure 670 shows a nucleotide sequence (SEQ ID NO : 670) of a native sequence PR037994 cDNA, a clone designated herein as "DNA227531".

Figure 671 shows the amino acid sequence (SEQ ID NO : 671) derived from the coding sequence of Figure 670.

Figure 672 shows a nucleotide sequence (SEQ ID NO : 672) of a native sequence PR083660 cDNA, a clone designated herein as "DNA327673".

Figure 673 shows the amino acid sequence (SEQ ID NO : 673) derived from the coding sequence of Figure 672.

Figure 674A-B shows a nucleotide sequence (SEQ ID NO : 674) of a native sequence PR083661 cDNA, a clone designated herein as "DNA327674".

Figure 675 shows the amino acid sequence (SEQ ID NO : 675) derived from the coding sequence of Figure 674A-B.

Figure 676 shows a nucleotide sequence (SEQ ID NO : 676) of a native sequence PR083662 cDNA, a clone designated herein as "DNA327675".

Figure 677 shows the amino acid sequence (SEQ ID NO : 677) derived from the coding sequence of Figure 676.

Figure 678 shows a nucleotide sequence (SEQ ID NO : 678) of a native sequence PR02040 cDNA, a clone designated herein as "DNA327676".

Figure 679 shows the amino acid sequence (SEQ ID NO : 679) derived from the coding sequence of Figure 678.

Figure 680A-B shows a nucleotide sequence (SEQ ID NO : 680) of a native sequence PR050849 cDNA, a clone designated herein as "DNA255794".

Figure 681 shows the amino acid sequence (SEQ ID NO : 681) derived from the coding sequence of Figure 680.

Figure 682 shows a nucleotide sequence (SEQ ID NO : 682) of a native sequence PR050985 cDNA, a clone designated herein as "DNA255933".

Figure 683 shows the amino acid sequence (SEQ ID NO : 683) derived from the coding sequence of Figure 682.

Figure 684 shows a nucleotide sequence (SEQ ID NO : 684) of a native sequence PR050984 cDNA,

a clone designated herein as "DNA255850".

Figure 685 shows the amino acid sequence (SEQ ID NO : 685) derived from the coding sequence of Figure 684.

Figure 686 shows a nucleotide sequence (SEQ ID NO : 686) of a native sequence PR038131 cDNA, a clone designated herein as "DNA227668".

Figure 687 shows the amino acid sequence (SEQ ID NO : 687) derived from the coding sequence of Figure 686.

Figure 688 shows a nucleotide sequence (SEQ ID NO : 688) of a native sequence PR024015 cDNA, a clone designated herein as "DNA327677".

Figure 689 shows the amino acid sequence (SEQ ID NO : 689) derived from the coding sequence of Figure 688.

Figure 690 shows a nucleotide sequence (SEQ ID NO : 690) of a native sequence PR035066 cDNA, a clone designated herein as "DNA327678".

Figure 691 shows the amino acid sequence (SEQ ID NO : 691) derived from the coding sequence of Figure 690.

Figure 692 shows a nucleotide sequence (SEQ ID NO : 692) of a native sequence PR023864 cDNA, a clone designated herein as "DNA194506".

Figure 693 shows the amino acid sequence (SEQ ID NO : 693) derived from the coding sequence of Figure 692.

Figure 694 shows a nucleotide sequence (SEQ ID NO : 694) of a native sequence PR083663 cDNA, a clone designated herein as "DNA327679".

Figure 695 shows the amino acid sequence (SEQ ID NO : 695) derived from the coding sequence of Figure 694.

Figure 696 shows a nucleotide sequence (SEQ ID NO : 696) of a native sequence PR083664 cDNA, a clone designated herein as "DNA327680".

Figure 697 shows the amino acid sequence (SEQ ID NO : 697) derived from the coding sequence of Figure 696.

Figure 698A-C shows a nucleotide sequence (SEQ ID NO : 698) of a native sequence PR083665 cDNA, a clone designated herein as "DNA327681".

Figure 699 shows the amino acid sequence (SEQ ID NO : 699) derived from the coding sequence of Figure 698A-C.



Figure 700 shows a nucleotide sequence (SEQ ID NO : 700) of a native sequence PR083666 cDNA, a clone designated herein as "DNA327682".

Figure 701 shows the amino acid sequence (SEQ ID NO : 701) derived from the coding sequence of Figure 700.

Figure 702 shows a nucleotide sequence (SEQ ID NO : 702) of a native sequence PRO58590 cDNA, a clone designated herein as "DNA270202".

Figure 703 shows the amino acid sequence (SEQ ID NO : 703) derived from the coding sequence of Figure 702.

Figure 704 shows a nucleotide sequence (SEQ ID NO : 704) of a native sequence PR083667 cDNA, a clone designated herein as "DNA327683".

Figure 705 shows the amino acid sequence (SEQ ID NO : 705) derived from the coding sequence of Figure 704.

Figure 706A-B shows a nucleotide sequence (SEQ ID NO : 706) of a native sequence PRO83668 cDNA, a clone designated herein as "DNA327684".

Figure 707 shows the amino acid sequence (SEQ ID NO : 707) derived from the coding sequence of Figure 706A-B.

Figure 708 shows a nucleotide sequence (SEQ ID NO : 708) of a native sequence PRO83669 cDNA, a clone designated herein as "DNA327685".

Figure 709 shows the amino acid sequence (SEQ ID NO : 709) derived from the coding sequence of Figure 708.

Figure 710 shows a nucleotide sequence (SEQ ID NO : 710) of a native sequence PR083670 cDNA, a clone designated herein as "DNA327686".

Figure 711 shows the amino acid sequence (SEQ ID NO : 711) derived from the coding sequence of Figure 710.

Figure 712 shows a nucleotide sequence (SEQ ID NO : 712) of a native sequence PRO83671 cDNA, a clone designated herein as "DNA327687".

Figure 713 shows the amino acid sequence (SEQ ID NO : 713) derived from the coding sequence of Figure 712.

Figure 714 shows a nucleotide sequence (SEQ ID NO : 714) of a native sequence PRO83672 cDNA, a clone designated herein as "DNA327688".

Figure 715 shows the amino acid sequence (SEQ ID NO : 715) derived from the coding sequence of

Figure 714.

Figure 716A-B shows a nucleotide sequence (SEQ ID NO : 716) of a native sequence PR082391 cD 716 is a clone designated herein as "DNA325944".

Figure 717 shows the amino acid sequence (SEQ ID NO : 717) derived from the coding sequence of Figure 716A-B.

Figure 718 shows a nucleotide sequence (SEQ ID NO : 718) of a native sequence PR09824 cDNA, v clone designated herein as "DNA327689".

Figure 719 shows the amino acid sequence (SEQ ID NO : 719) derived from the coding sequence of Figure 718.

Figure 720 shows a nucleotide sequence (SEQ ID NO : 720) of a native sequence PR083673 cDNA, a clone designated herein as "DNA327690".

Figure 721 shows the amino acid sequence (SEQ ID NO : 721) derived from the coding sequence of Figure 720.

Figure 722 shows a nucleotide sequence (SEQ ID NO : 722) of a native sequence PR083674 cDNA, a clone designated herein as "DNA327691".

Figure 723 shows the amino acid sequence (SEQ ID NO : 723) derived from the coding sequence of Figure 722.

Figure 724 shows a nucleotide sequence (SEQ ID NO : 724) of a native sequence PR083675 cDNA, a clone designated herein as "DNA327692".

Figure 725 shows the amino acid sequence (SEQ ID NO : 725) derived from the coding sequence of Figure 724.

Figure 726A-C shows a nucleotide sequence (SEQ ID NO : 726) of a native sequence PR083676 cD 726 is a clone designated herein as "DNA327693".

Figure 727 shows the amino acid sequence (SEQ ID NO : 727) derived from the coding sequence of Figure 726A-C.

Figure 728A-C shows a nucleotide sequence (SEQ ID NO : 728) of a native sequence PR083677 cD 728 is a clone designated herein as "DNA327694".

Figure 729 shows the amino acid sequence (SEQ ID NO : 729) derived from the coding sequence of Figure 728A-C.

Figure 730A-C shows a nucleotide sequence (SEQ ID NO : 730) of a native sequence PR083678 cD 730 is a clone designated herein as "DNA327695".

Figure 731 shows the amino acid sequence (SEQ ID NO : 731) derived from the coding sequence of Figure 730A-C.

Figure 732A-B shows a nucleotide sequence (SEQ ID NO : 732) of a native sequence PR04870 cDN is a clone designated herein as "DNA325513".

Figure 733 shows the amino acid sequence (SEQ ID NO : 733) derived from the coding sequence of Figure 732A-B.

Figure 734 shows a nucleotide sequence (SEQ ID NO : 734) of a native sequence PR083679 cDNA, a clone designated herein as "DNA327696".

Figure 735 shows the amino acid sequence (SEQ ID NO : 735) derived from the coding sequence of Figure 734.

Figure 736 shows a nucleotide sequence (SEQ ID NO : 736) of a native sequence PR062376 cDNA, a clone designated herein as "DNA274471".

Figure 737 shows the amino acid sequence (SEQ ID NO : 737) derived from the coding sequence of Figure 736.

Figure 738 shows a nucleotide sequence (SEQ ID NO : 738) of a native sequence PR083680 cDNA, a clone designated herein as "DNA327697".

Figure 739 shows the amino acid sequence (SEQ ID NO : 739) derived from the coding sequence of Figure 738.

Figure 740 shows a nucleotide sequence (SEQ ID NO : 740) of a native sequence PR083681 cDNA, a clone designated herein as "DNA327698".

Figure 741 shows the amino acid sequence (SEQ ID NO : 741) derived from the coding sequence of Figure 740.

Figure 742 shows a nucleotide sequence (SEQ ID NO : 742) of a native sequence PR083682 cDNA, a clone designated herein as "DNA327699".

Figure 743 shows the amino acid sequence (SEQ ID NO : 743) derived from the coding sequence of Figure 742.

Figure 744A-B shows a nucleotide sequence (SEQ ID NO : 744) of a native sequence PR02564 cDN is a clone designated herein as "DNA83031".

Figure 745 shows the amino acid sequence (SEQ ID NO : 745) derived from the coding sequence of Figure 744A-B.

Figure 746 shows a nucleotide sequence (SEQ ID NO : 746) of a native sequence PR083683 cDNA

a clone designated herein as "DNA327700".

Figure 747 shows the amino acid sequence (SEQ ID NO : 747) derived from the coding sequence of Figure 746.

Figure 748 shows a nucleotide sequence (SEQ ID NO : 748) of a native sequence PRO82667 cDNA, a clone designated herein as "DNA327701".

Figure 749 shows the amino acid sequence (SEQ ID NO : 749) derived from the coding sequence of Figure 748.

Figure 750 shows a nucleotide sequence (SEQ ID NO : 750) of a native sequence PRO83684 cDNA, a clone designated herein as "DNA327702".

Figure 751 shows the amino acid sequence (SEQ ID NO : 751) derived from the coding sequence of Figure 750.

Figure 752 shows a nucleotide sequence (SEQ ID NO : 752) of a native sequence PRO83685 cDNA, a clone designated herein as "DNA327703".

Figure 753 shows the amino acid sequence (SEQ ID NO : 753) derived from the coding sequence of Figure 752.

Figure 754 shows a nucleotide sequence (SEQ ID NO : 754) of a native sequence PRO58048 cDNA, a clone designated herein as "DNA269636".

Figure 755 shows the amino acid sequence (SEQ ID NO : 755) derived from the coding sequence of Figure 754.

Figure 756A-B shows a nucleotide sequence (SEQ ID NO : 756) of a native sequence PRO81999 cD 756 is a clone designated herein as "DNA325478".

Figure 757 shows the amino acid sequence (SEQ ID NO : 757) derived from the coding sequence of Figure 756A-B.

Figure 758 shows a nucleotide sequence (SEQ ID NO : 758) of a native sequence PRO83686 cDNA, a clone designated herein as "DNA327704".

Figure 759 shows the amino acid sequence (SEQ ID NO : 759) derived from the coding sequence of Figure 758.

Figure 760 shows a nucleotide sequence (SEQ ID NO : 760) of a native sequence PRO83687 cDNA, a clone designated herein as "DNA327705".

Figure 761 shows the amino acid sequence (SEQ ID NO : 761) derived from the coding sequence of Figure 760.

Figure 762 shows a nucleotide sequence (SEQ ID NO : 762) of a native sequence PR083688 cDNA, a clone designated herein as "DNA327706".

Figure 763 shows the amino acid sequence (SEQ ID NO : 763) derived from the coding sequence of Figure 762.

Figure 764 shows a nucleotide sequence (SEQ ID NO : 764) of a native sequence PR037752 cDNA, a clone designated herein as "DNA227289".

Figure 765 shows the amino acid sequence (SEQ ID NO : 765) derived from the coding sequence of Figure 764.

Figure 766 shows a nucleotide sequence (SEQ ID NO : 766) of a native sequence PRO83689 cDNA, a clone designated herein as "DNA327707".

Figure 767 shows the amino acid sequence (SEQ ID NO : 767) derived from the coding sequence of Figure 766.

Figure 768 shows a nucleotide sequence (SEQ ID NO : 768) of a native sequence cDNA, wherein SE designated herein as "DNA327708".

Figure 769 shows a nucleotide sequence (SEQ ID NO : 769) of a native sequence PR021716 cDNA, a clone designated herein as "DNA188204".

Figure 770 shows the amino acid sequence (SEQ ID NO : 770) derived from the coding sequence of Figure 769.

Figure 771 shows a nucleotide sequence (SEQ ID NO : 771) of a native sequence PRO83690 cDNA, a clone designated herein as "DNA327709".

Figure 772 shows the amino acid sequence (SEQ ID NO : 772) derived from the coding sequence of Figure 771.

Figure 773 shows a nucleotide sequence (SEQ ID NO : 773) of a native sequence PR081730 cDNA, a clone designated herein as "DNA325163".

Figure 774 shows the amino acid sequence (SEQ ID NO : 774) derived from the coding sequence of Figure 773.

Figure 775 shows a nucleotide sequence (SEQ ID NO : 775) of a native sequence PRO83691 cDNA, a clone designated herein as "DNA327710".

Figure 776 shows the amino acid sequence (SEQ ID NO : 776) derived from the coding sequence of Figure 775.

Figure 777 shows a nucleotide sequence (SEQ ID NO : 777) of a native sequence PRO83692 cDNA

a clone designated herein as "DNA32771".

Figure 778 shows the amino acid sequence (SEQ ID NO : 778) derived from the coding sequence of Figure 777.

Figure 779 shows a nucleotide sequence (SEQ ID NO : 779) of a native sequence PR011113 cDNA, a clone designated herein as "DNA327712".

Figure 780 shows the amino acid sequence (SEQ ID NO : 780) derived from the coding sequence of Figure 779.

Figure 781 shows a nucleotide sequence (SEQ ID NO : 781) of a native sequence PR037975 cDNA, a clone designated herein as "DNA327713".

Figure 782 shows the amino acid sequence (SEQ ID NO : 782) derived from the coding sequence of Figure 781.

Figure 783 shows a nucleotide sequence (SEQ ID NO : 783) of a native sequence PR081832 cDNA, a clone designated herein as "DNA325285".

Figure 784 shows the amino acid sequence (SEQ ID NO : 784) derived from the coding sequence of Figure 783.

Figure 785A-B shows a nucleotide sequence (SEQ ID NO : 785) of a native sequence PR083693 cDNA, a clone designated herein as "DNA327714".

Figure 786 shows the amino acid sequence (SEQ ID NO : 786) derived from the coding sequence of Figure 785.

Figure 787 shows a nucleotide sequence (SEQ ID NO : 787) of a native sequence PRO83694 cDNA, a clone designated herein as "DNA327715".

Figure 788 shows the amino acid sequence (SEQ ID NO : 788) derived from the coding sequence of Figure 787.

Figure 789 shows a nucleotide sequence (SEQ ID NO : 789) of a native sequence PRO82674 cDNA, a clone designated herein as "DNA326267".

Figure 790 shows the amino acid sequence (SEQ ID NO : 790) derived from the coding sequence of Figure 789.

Figure 791 shows a nucleotide sequence (SEQ ID NO : 791) of a native sequence PR04766 cDNA, a clone designated herein as "DNA103439".

Figure 792 shows the amino acid sequence (SEQ ID NO : 792) derived from the coding sequence of Figure 791.

Figure 793 shows a nucleotide sequence (SEQ ID NO : 793) of a native sequence PR037946 cDNA, a clone designated herein as "DNA227483".

Figure 794 shows the amino acid sequence (SEQ ID NO : 794) derived from the coding sequence of Figure 793.

Figure 795 shows a nucleotide sequence (SEQ ID NO : 795) of a native sequence PR061496 cDNA, a clone designated herein as "DNA273515".

Figure 796 shows the amino acid sequence (SEQ ID NO : 796) derived from the coding sequence of Figure 795.

Figure 797 shows a nucleotide sequence (SEQ ID NO : 797) of a native sequence PRO83695 cDNA, a clone designated herein as "DNA327716".

Figure 798 shows the amino acid sequence (SEQ ID NO : 798) derived from the coding sequence of Figure 797.

Figure 799 shows a nucleotide sequence (SEQ ID NO : 799) of a native sequence PR062702 cDNA, a clone designated herein as "DNA274969".

Figure 800 shows the amino acid sequence (SEQ ID NO : 800) derived from the coding sequence of Figure 799.

Figure 801 shows a nucleotide sequence (SEQ ID NO : 801) of a native sequence PRO83696 cDNA, a clone designated herein as "DNA327717".

Figure 802 shows the amino acid sequence (SEQ ID NO : 802) derived from the coding sequence of Figure 801.

Figure 803 shows a nucleotide sequence (SEQ ID NO : 803) of a native sequence cDNA, wherein SE designated herein as "DNA274406".

Figure 804 shows a nucleotide sequence (SEQ ID NO : 804) of a native sequence PRO83697 cDNA, a clone designated herein as "DNA327718".

Figure 805 shows the amino acid sequence (SEQ ID NO : 805) derived from the coding sequence of Figure 804.

Figure 806 shows a nucleotide sequence (SEQ ID NO : 806) of a native sequence PRO58042 cDNA, a clone designated herein as "DNA269630".

Figure 807 shows the amino acid sequence (SEQ ID NO : 807) derived from the coding sequence of Figure 806.

Figure 808 shows a nucleotide sequence (SEQ ID NO : 808) of a native sequence PRO83698 cDNA,

a clone designated herein as "DNA327719".

Figure 809 shows the amino acid sequence (SEQ ID NO : 809) derived from the coding sequence of Figure 808.

Figure 810 shows a nucleotide sequence (SEQ ID NO : 810) of a native sequence PR083699 cDNA, a clone designated herein as "DNA327720".

Figure 811 shows the amino acid sequence (SEQ ID NO : 811) derived from the coding sequence of Figure 810.

Figure 812 shows a nucleotide sequence (SEQ ID NO : 812) of a native sequence PRO81429 cDNA, a clone designated herein as "DNA324816".

Figure 813 shows the amino acid sequence (SEQ ID NO : 813) derived from the coding sequence of Figure 812.

Figure 814 shows a nucleotide sequence (SEQ ID NO : 814) of a native sequence PRO83700 cDNA, a clone designated herein as "DNA327721".

Figure 815 shows the amino acid sequence (SEQ ID NO : 815) derived from the coding sequence of Figure 814.

Figure 816 shows a nucleotide sequence (SEQ ID NO : 816) of a native sequence PR036415 cDNA, a clone designated herein as "DNA225952".

Figure 817 shows the amino acid sequence (SEQ ID NO : 817) derived from the coding sequence of Figure 816.

Figure 818 shows a nucleotide sequence (SEQ ID NO : 818) of a native sequence PRO83701 cDNA, is a clone designated herein as "DNA327722".

Figure 819 shows the amino acid sequence (SEQ ID NO : 819) derived from the coding sequence of Figure 818.

Figure 820 shows a nucleotide sequence (SEQ ID NO : 820) of a native sequence PR061971 cDNA, a clone designated herein as "DNA274027".

Figure 821 shows the amino acid sequence (SEQ ID NO : 821) derived from the coding sequence of Figure 820.

Figure 822 shows a nucleotide sequence (SEQ ID NO : 822) of a native sequence PR083702 cDNA, a clone designated herein as "DNA327723".

Figure 823 shows the amino acid sequence (SEQ ID NO : 823) derived from the coding sequence of Figure 822.



Figure 824 shows a nucleotide sequence (SEQ ID NO : 824) of a native sequence cDNA, wherein S designated herein as "DNA327724".

Figure 825 shows a nucleotide sequence (SEQ ID NO : 825) of a native sequence PR059053 cDNA a clone designated herein as "DNA270689".

Figure 826 shows the amino acid sequence (SEQ ID NO : 826) derived from the coding sequence of Figure 825.

Figure 827 shows a nucleotide sequence (SEQ ID NO : 827) of a native sequence PR083703 cDNA a clone designated herein as "DNA327725".

Figure 828 shows the amino acid sequence (SEQ ID NO : 828) derived from the coding sequence of Figure 827.

Figure 829A-B shows a nucleotide sequence (SEQ ID NO : 829) of a native sequence PR083704 cDNA a clone designated herein as "DNA327726".

Figure 830 shows the amino acid sequence (SEQ ID NO : 830) derived from the coding sequence of Figure 829A-B.

Figure 831 shows a nucleotide sequence (SEQ ID NO : 831) of a native sequence PR083705 cDNA a clone designated herein as "DNA327727".

Figure 832 shows the amino acid sequence (SEQ ID NO : 832) derived from the coding sequence of Figure 831.

Figure 833 shows a nucleotide sequence (SEQ ID NO : 833) of a native sequence PR04348 cDNA a clone designated herein as "DNA327728".

Figure 834 shows the amino acid sequence (SEQ ID NO : 834) derived from the coding sequence of Figure 833.

Figure 835 shows a nucleotide sequence (SEQ ID NO : 835) of a native sequence PR036908 cDNA a clone designated herein as "DNA226445".

Figure 836 shows the amino acid sequence (SEQ ID NO : 836) derived from the coding sequence of Figure 835.

Figure 837 shows a nucleotide sequence (SEQ ID NO : 837) of a native sequence PR062893 cDNA a clone designated herein as "DNA275195".

Figure 838 shows the amino acid sequence (SEQ ID NO : 838) derived from the coding sequence of Figure 837.

Figure 839 shows a nucleotide sequence (SEQ ID NO : 839) of a native sequence PR058354 cDNA

a clone designated herein as "DNA327729".

Figure 840 shows the amino acid sequence (SEQ ID NO : 840) derived from the coding sequence of Figure 839.

Figure 841 shows a nucleotide sequence (SEQ ID NO : 841) of a native sequence PR083706 cDNA, a clone designated herein as "DNA327730".

Figure 842 shows the amino acid sequence (SEQ ID NO : 842) derived from the coding sequence of Figure 841.

Figure 843 shows a nucleotide sequence (SEQ ID NO : 843) of a native sequence PR083707 cDNA, a clone designated herein as "DNA327731".

Figure 844 shows the amino acid sequence (SEQ ID NO : 844) derived from the coding sequence of Figure 843.

Figure 845 shows a nucleotide sequence (SEQ ID NO : 845) of a native sequence PR061801 cDNA, a clone designated herein as "DNA327732".

Figure 846 shows the amino acid sequence (SEQ ID NO : 846) derived from the coding sequence of Figure 845.

Figure 847A-B shows a nucleotide sequence (SEQ ID NO : 847) of a native sequence PRO83708 cDNA, a clone designated herein as "DNA327733".

Figure 848 shows the amino acid sequence (SEQ ID NO : 848) derived from the coding sequence of Figure 847.

Figure 849 shows a nucleotide sequence (SEQ ID NO : 849) of a native sequence PRO83709 cDNA, a clone designated herein as "DNA327734".

Figure 850 shows the amino acid sequence (SEQ ID NO : 850) derived from the coding sequence of Figure 849.

Figure 851 shows a nucleotide sequence (SEQ ID NO : 851) of a native sequence PRO83710 cDNA, a clone designated herein as "DNA327735".

Figure 852 shows the amino acid sequence (SEQ ID NO : 852) derived from the coding sequence of Figure 851.

Figure 853 shows a nucleotide sequence (SEQ ID NO : 853) of a native sequence PR070858 cDNA, a clone designated herein as "DNA299884".

Figure 854 shows the amino acid sequence (SEQ ID NO : 854) derived from the coding sequence of Figure 853.

Figure 855 shows a nucleotide sequence (SEQ ID NO : 855) of a native sequence PR02601 cDNA, w  
clone designated herein as "DNA83128".

Figure 856 shows the amino acid sequence (SEQ ID NO : 856) derived from the coding sequence of :  
Figure 855.

Figure 857 shows a nucleotide sequence (SEQ ID NO : 857) of a native sequence PR083711 cDNA,  
a clone designated herein as "DNA327736".

Figure 858 shows the amino acid sequence (SEQ ID NO : 858) derived from the coding sequence of :  
Figure 857.

Figure 859 shows a nucleotide sequence (SEQ ID NO : 859) of a native sequence PR083712 cDNA,  
a clone designated herein as "DNA327737".

Figure 860 shows the amino acid sequence (SEQ ID NO : 860) derived from the coding sequence of :  
Figure 859.

Figure 861 shows a nucleotide sequence (SEQ ID NO : 861) of a native sequence PR083713 cDNA,  
a clone designated herein as "DNA327738".

Figure 862 shows the amino acid sequence (SEQ ID NO : 862) derived from the coding sequence of :  
Figure 861.

Figure 863 shows a nucleotide sequence (SEQ ID NO : 863) of a native sequence PR083714 cDNA,  
a clone designated herein as "DNA327739".

Figure 864 shows the amino acid sequence (SEQ ID NO : 864) derived from the coding sequence of :  
Figure 863.

Figure 865 shows a nucleotide sequence (SEQ ID NO : 865) of a native sequence PRO1787 cDNA, w  
clone designated herein as "DNA327740".

Figure 866 shows the amino acid sequence (SEQ ID NO : 866) derived from the coding sequence of :  
Figure 865.

Figure 867 shows a nucleotide sequence (SEQ ID NO : 867) of a native sequence PRO83715 cDNA,  
a clone designated herein as "DNA327741".

Figure 868 shows the amino acid sequence (SEQ ID NO : 868) derived from the coding sequence of :  
Figure 867.

Figure 869 shows a nucleotide sequence (SEQ ID NO : 869) of a native sequence PR058969 cDNA,  
a clone designated herein as "DNA270597".

Figure 870 shows the amino acid sequence (SEQ ID NO : 870) derived from the coding sequence of :

Figure 869.

Figure 871A-D shows a nucleotide sequence (SEQ ID NO : 871) of a native sequence PR083716 c 871 is a clone designated herein as "DNA327742".

Figure 872A-B shows the amino acid sequence (SEQ ID NO : 872) derived from the coding sequence in Figure 871A-D.

Figure 873 shows a nucleotide sequence (SEQ ID NO : 873) of a native sequence PR083717 cDN; a clone designated herein as "DNA327743".

Figure 874 shows the amino acid sequence (SEQ ID NO : 874) derived from the coding sequence c Figure 873.

Figure 875 shows a nucleotide sequence (SEQ ID NO : 875) of a native sequence PR060945 cDN; a clone designated herein as "DNA326821".

Figure 876 shows the amino acid sequence (SEQ ID NO : 876) derived from the coding sequence c Figure 875.

Figure 877 shows a nucleotide sequence (SEQ ID NO : 877) of a native sequence PR071063 cDN; a clone designated herein as "DNA304499".

Figure 878 shows the amino acid sequence (SEQ ID NO : 878) derived from the coding sequence c Figure 877.

Figure 879 shows a nucleotide sequence (SEQ ID NO : 879) of a native sequence PR083718 cDN; a clone designated herein as "DNA327744".

Figure 880 shows the amino acid sequence (SEQ ID NO : 880) derived from the coding sequence c Figure 879.

Figure 881 shows a nucleotide sequence (SEQ ID NO : 881) of a native sequence PR083719 cDN; a clone designated herein as "DNA327745".

Figure 882 shows the amino acid sequence (SEQ ID NO : 882) derived from the coding sequence c Figure 881.

Figure 883 shows a nucleotide sequence (SEQ ID NO : 883) of a native sequence PR083720 cDN; a clone designated herein as "DNA327746".

Figure 884 shows the amino acid sequence (SEQ ID NO : 884) derived from the coding sequence c Figure 883.

Figure 885 shows a nucleotide sequence (SEQ ID NO : 885) of a native sequence PR025204 cDN; a clone designated herein as "DNA196754".

Figure 886 shows the amino acid sequence (SEQ ID NO : 886) derived from the coding sequence of Figure 885.

Figure 887 shows a nucleotide sequence (SEQ ID NO : 887) of a native sequence PR060397 cDNA, a clone designated herein as "DNA272127".

Figure 888 shows the amino acid sequence (SEQ ID NO : 888) derived from the coding sequence of Figure 887.

Figure 889 shows a nucleotide sequence (SEQ ID NO : 889) of a native sequence PR083721 cDNA, a clone designated herein as "DNA327747".

Figure 890 shows the amino acid sequence (SEQ ID NO : 890) derived from the coding sequence of Figure 889.

Figure 891 shows a nucleotide sequence (SEQ ID NO : 891) of a native sequence PR04575 cDNA, a clone designated herein as "DNA103245".

Figure 892 shows the amino acid sequence (SEQ ID NO : 892) derived from the coding sequence of Figure 891.

Figure 893 shows a nucleotide sequence (SEQ ID NO : 893) of a native sequence PR037550 cDNA, a clone designated herein as "DNA227087".

Figure 894 shows the amino acid sequence (SEQ ID NO : 894) derived from the coding sequence of Figure 893.

Figure 895 shows a nucleotide sequence (SEQ ID NO : 895) of a native sequence PR036541 cDNA, a clone designated herein as "DNA226078".

Figure 896 shows the amino acid sequence (SEQ ID NO : 896) derived from the coding sequence of Figure 895.

Figure 897A-B shows a nucleotide sequence (SEQ ID NO : 897) of a native sequence PR02537 cDNA, is a clone designated herein as "DNA76504".

Figure 898 shows the amino acid sequence (SEQ ID NO : 898) derived from the coding sequence of Figure 897A-B.

Figure 899 shows a nucleotide sequence (SEQ ID NO : 899) of a native sequence PR083722 cDNA, a clone designated herein as "DNA327748".

Figure 900 shows the amino acid sequence (SEQ ID NO : 900) derived from the coding sequence of Figure 899.

Figure 901 shows a nucleotide sequence (SEQ ID NO : 901) of a native sequence PR083723 cDNA

a clone designated herein as "DNA327749".

Figure 902 shows the amino acid sequence (SEQ ID NO : 902) derived from the coding sequence of Figure 901.

Figure 903 shows a nucleotide sequence (SEQ ID NO : 903) of a native sequence PR083724 cDNA, a clone designated herein as "DNA327750".

Figure 904 shows the amino acid sequence (SEQ ID NO : 904) derived from the coding sequence of Figure 903.

Figure 905 shows a nucleotide sequence (SEQ ID NO : 905) of a native sequence PR061480 cDNA, a clone designated herein as "DNA327751".

Figure 906 shows the amino acid sequence (SEQ ID NO : 906) derived from the coding sequence of Figure 905.

Figure 907 shows a nucleotide sequence (SEQ ID NO : 907) of a native sequence PR02695 cDNA, w clone designated herein as "DNA88198".

Figure 908 shows the amino acid sequence (SEQ ID NO : 908) derived from the coding sequence of Figure 907.

Figure 909 shows a nucleotide sequence (SEQ ID NO : 909) of a native sequence cDNA, wherein SE designated herein as "DNA327752".

Figure 910 shows a nucleotide sequence (SEQ ID NO : 910) of a native sequence PR020144 cDNA, a clone designated herein as "DNA171416".

Figure 911 shows the amino acid sequence (SEQ ID NO : 911) derived from the coding sequence of Figure 910.

Figure 912 shows a nucleotide sequence (SEQ ID NO : 912) of a native sequence PR051365 cDNA, a clone designated herein as "DNA327753".

Figure 913 shows the amino acid sequence (SEQ ID NO : 913) derived from the coding sequence of Figure 912.

Figure 914 shows a nucleotide sequence (SEQ ID NO : 914) of a native sequence PR04526 cDNA, w clone designated herein as "DNA327754".

Figure 915 shows the amino acid sequence (SEQ ID NO : 915) derived from the coding sequence of Figure 914.

Figure 916 shows a nucleotide sequence (SEQ ID NO : 916) of a native sequence PR083725 cDNA, a clone designated herein as "DNA327755".

Figure 917 shows the amino acid sequence (SEQ ID NO : 917) derived from the coding sequence of Figure 916.

Figure 918 shows a nucleotide sequence (SEQ ID NO : 918) of a native sequence PR083726 cDNA, a clone designated herein as "DNA327756".

Figure 919 shows the amino acid sequence (SEQ ID NO : 919) derived from the coding sequence of Figure 918.

Figure 920A-B shows a nucleotide sequence (SEQ ID NO : 920) of a native sequence PR060082 cDI 920 is a clone designated herein as "DNA327757".

Figure 921 shows the amino acid sequence (SEQ ID NO : 921) derived from the coding sequence of Figure 920A-B.

Figure 922 shows a nucleotide sequence (SEQ ID NO : 922) of a native sequence PR081272 cDNA, a clone designated herein as "DNA324626".

Figure 923 shows the amino acid sequence (SEQ ID NO : 923) derived from the coding sequence of Figure 922.

Figure 924A-D shows a nucleotide sequence (SEQ ID NO : 924) of a native sequence PR083727 cDI 924 is a clone designated herein as "DNA327758".

Figure 925 shows the amino acid sequence (SEQ ID NO : 925) derived from the coding sequence of Figure 924A-D.

Figure 926 shows a nucleotide sequence (SEQ ID NO : 926) of a native sequence PRO83728 cDNA, a clone designated herein as "DNA327759".

Figure 927 shows the amino acid sequence (SEQ ID NO : 927) derived from the coding sequence of Figure 926.

Figure 928 shows a nucleotide sequence (SEQ ID NO : 928) of a native sequence PR059647 cDNA, a clone designated herein as "DNA271344".

Figure 929 shows the amino acid sequence (SEQ ID NO : 929) derived from the coding sequence of Figure 928.

Figure 930 shows a nucleotide sequence (SEQ ID NO : 930) of a native sequence PRO80955 cDNA, a clone designated herein as "DNA324272".

Figure 931 shows the amino acid sequence (SEQ ID NO : 931) derived from the coding sequence of Figure 930.

Figure 932 shows a nucleotide sequence (SEQ ID NO : 932) of a native sequence PR021787 cDNA

a clone designated herein as "DNA188293".

Figure 933 shows the amino acid sequence (SEQ ID NO : 933) derived from the coding sequence of Figure 932.

Figure 934 shows a nucleotide sequence (SEQ ID NO : 934) of a native sequence PRO83729 cDNA, a clone designated herein as "DNA327760".

Figure 935 shows the amino acid sequence (SEQ ID NO : 935) derived from the coding sequence of Figure 934.

Figure 936 shows a nucleotide sequence (SEQ ID NO : 936) of a native sequence PRO83730 cDNA, a clone designated herein as "DNA327761".

Figure 937 shows the amino acid sequence (SEQ ID NO : 937) derived from the coding sequence of Figure 936.

Figure 938 shows a nucleotide sequence (SEQ ID NO : 938) of a native sequence cDNA, wherein SE designated herein as "DNA327762".

Figure 939 shows a nucleotide sequence (SEQ ID NO : 939) of a native sequence PRO83731 cDNA, a clone designated herein as "DNA327763".

Figure 940 shows the amino acid sequence (SEQ ID NO : 940) derived from the coding sequence of Figure 939.

Figure 941 shows a nucleotide sequence (SEQ ID NO : 941) of a native sequence cDNA, wherein SE designated herein as "DNA327764".

Figure 942A-C shows a nucleotide sequence (SEQ ID NO : 942) of a native sequence PRO83732 cD 942 is a clone designated herein as "DNA327765".

Figure 943 shows the amino acid sequence (SEQ ID NO : 943) derived from the coding sequence of Figure 942A-C.

Figure 944A-B shows a nucleotide sequence (SEQ ID NO : 944) of a native sequence cDNA, whereir designated herein as "DNA194332".

Figure 945 shows a nucleotide sequence (SEQ ID NO : 945) of a native sequence PRO869690 cDNA, a clone designated herein as "DNA287433".

Figure 946 shows the amino acid sequence (SEQ ID NO : 946) derived from the coding sequence of Figure 945.

Figure 947 shows a nucleotide sequence (SEQ ID NO : 947) of a native sequence PRO83733 cDNA, a clone designated herein as "DNA327766".



Figure 948 shows the amino acid sequence (SEQ ID NO : 948) derived from the coding sequence of Figure 947.

Figure 949A-B shows a nucleotide sequence (SEQ ID NO : 949) of a native sequence PRO83734 cD 949 is a clone designated herein as "DNA327767".

Figure 950 shows the amino acid sequence (SEQ ID NO : 950) derived from the coding sequence of Figure 949A-B.

Figure 951 shows a nucleotide sequence (SEQ ID NO : 951) of a native sequence PR0119 cDNA, wt clone designated herein as "DNA52750".

Figure 952 shows the amino acid sequence (SEQ ID NO : 952) derived from the coding sequence of Figure 951.

Figure 953 shows a nucleotide sequence (SEQ ID NO : 953) of a native sequence cDNA, wherein SE designated herein as "DNA327768".

Figure 954 shows a nucleotide sequence (SEQ ID NO : 954) of a native sequence PRO83735 cDNA, a clone designated herein as "DNA327769".

Figure 955 shows the amino acid sequence (SEQ ID NO : 955) derived from the coding sequence of Figure 954.

Figure 956 shows a nucleotide sequence (SEQ ID NO : 956) of a native sequence PRO83736 cDNA, a clone designated herein as "DNA327770".

Figure 957 shows the amino acid sequence (SEQ ID NO : 957) derived from the coding sequence of Figure 956.

Figure 958 shows a nucleotide sequence (SEQ ID NO : 958) of a native sequence PRO12179 cDNA, a clone designated herein as "DNA151120".

Figure 959 shows the amino acid sequence (SEQ ID NO : 959) derived from the coding sequence of Figure 958.

Figure 960 shows a nucleotide sequence (SEQ ID NO : 960) of a native sequence PRO83737 cDNA, a clone designated herein as "DNA327771".

Figure 961 shows the amino acid sequence (SEQ ID NO : 961) derived from the coding sequence of Figure 960.

Figure 962A-B shows a nucleotide sequence (SEQ ID NO : 962) of a native sequence cDNA, wherein designated herein as "DNA228024".

Figure 963 shows a nucleotide sequence (SEQ ID NO : 963) of a native sequence cDNA wherein SE

designated herein as "DNA150980".

Figure 964 shows a nucleotide sequence (SEQ ID NO : 964) of a native sequence cDNA, wherein designated herein as "DNA327772".

Figure 965A-B shows a nucleotide sequence (SEQ ID NO : 965) of a native sequence PRO83739 965 is a clone designated herein as "DNA327773".

Figure 966 shows the amino acid sequence (SEQ ID NO : 966) derived from the coding sequence Figure 965.

Figure 967 shows a nucleotide sequence (SEQ ID NO : 967) of a native sequence PRO83740 cDNA a clone designated herein as "DNA327774".

Figure 968 shows the amino acid sequence (SEQ ID NO : 968) derived from the coding sequence Figure 967.

Figure 969A-C shows a nucleotide sequence (SEQ ID NO : 969) of a native sequence PRO83741 969 is a clone designated herein as "DNA327775".

Figure 970 shows the amino acid sequence (SEQ ID NO : 970) derived from the coding sequence Figure 969A-C.

Figure 971A-B shows a nucleotide sequence (SEQ ID NO : 971) of a native sequence PRO49304 cDNA 971 is a clone designated herein as "DNA254192".

Figure 972 shows the amino acid sequence (SEQ ID NO : 972) derived from the coding sequence Figure 971A-B.

Figure 973A-B shows a nucleotide sequence (SEQ ID NO : 973) of a native sequence PRO62241 cDNA 973 is a clone designated herein as "DNA274322".

Figure 974 shows the amino acid sequence (SEQ ID NO : 974) derived from the coding sequence Figure 973A-B.

Figure 975 shows a nucleotide sequence (SEQ ID NO : 975) of a native sequence PRO36504 cDNA a clone designated herein as "DNA226041".

Figure 976 shows the amino acid sequence (SEQ ID NO : 976) derived from the coding sequence Figure 975.

Figure 977 shows a nucleotide sequence (SEQ ID NO : 977) of a native sequence PRO83742 cDNA a clone designated herein as "DNA327776".

Figure 978 shows the amino acid sequence (SEQ ID NO : 978) derived from the coding sequence Figure 977.

Figure 979 shows a nucleotide sequence (SEQ ID NO : 979) of a native sequence PR011833 cDNA, a clone designated herein as "DNA151487".

Figure 980 shows the amino acid sequence (SEQ ID NO : 980) derived from the coding sequence of Figure 979.

Figure 981A-D shows a nucleotide sequence (SEQ ID NO : 981) of a native sequence cDNA, whereir designated herein as "DNA327777".

Figure 982A-B shows a nucleotide sequence (SEQ ID NO : 982) of a native sequence cDNA, whereir designated herein as "DNA327778".

Figure 983A-B shows a nucleotide sequence (SEQ ID NO : 983) of a native sequence cDNA, whereir designated herein as "DNA270118".

Figure 984A-B shows a nucleotide sequence (SEQ ID NO : 984) of a native sequence PR083744 cD 984 is a clone designated herein as "DNA327779".

Figure 985 shows the amino acid sequence (SEQ ID NO : 985) derived from the coding sequence of Figure 984A-B.

Figure 986A-B shows a nucleotide sequence (SEQ ID NO : 986) of a native sequence cDNA, whereir designated herein as "DNA327780".

Figure 987A-B shows a nucleotide sequence (SEQ ID NO : 987) of a native sequence PR083745 cD 987 is a clone designated herein as "DNA327781".

Figure 988 shows the amino acid sequence (SEQ ID NO : 988) derived from the coding sequence of Figure 987A-B.

Figure 989 shows a nucleotide sequence (SEQ ID NO : 989) of a native sequence cDNA, wherein SE designated herein as "DNA327782".

Figure 990 shows a nucleotide sequence (SEQ ID NO : 990) of a native sequence PR083747 cDNA, a clone designated herein as "DNA327783".

Figure 991 shows the amino acid sequence (SEQ ID NO : 991) derived from the coding sequence of Figure 990.

Figure 992A-B shows a nucleotide sequence (SEQ ID NO : 992) of a native sequence PR083748 cD 992 is a clone designated herein as "DNA327784".

Figure 993 shows the amino acid sequence (SEQ ID NO : 993) derived from the coding sequence of Figure 992A-B.

Figure 994 shows a nucleotide sequence (SEQ ID NO : 994) of a native sequence PR083749 cDNA

a clone designated herein as "DNA323879".

Figure 995 shows the amino acid sequence (SEQ ID NO : 995) derived from the coding sequence of Figure 994.

Figure 996 shows a nucleotide sequence (SEQ ID NO : 996) of a native sequence PR083749 cDNA, a clone designated herein as "DNA327785".

Figure 997 shows the amino acid sequence (SEQ ID NO : 997) derived from the coding sequence of Figure 996.

Figure 998 shows a nucleotide sequence (SEQ ID NO : 998) of a native sequence cDNA, wherein SE designated herein as "DNA327786".

Figure 999 shows a nucleotide sequence (SEQ ID NO : 999) of a native sequence PR083751 cDNA, a clone designated herein as "DNA327787".

Figure 1000 shows the amino acid sequence (SEQ ID NO : 1000) derived from the coding sequence in Figure 999.

Figure 1001 shows a nucleotide sequence (SEQ ID NO : 1001) of a native sequence PR083752 cDN. 1001 is a clone designated herein as "DNA327788".

Figure 1002 shows the amino acid sequence (SEQ ID NO : 1002) derived from the coding sequence in Figure 1001.

Figure 1003 shows a nucleotide sequence (SEQ ID NO : 1003) of a native sequence cDNA, wherein designated herein as "DNA228053".

Figure 1004 shows a nucleotide sequence (SEQ ID NO : 1004) of a native sequence PR054720 cDN. 1004 is a clone designated herein as "DNA260974".

Figure 1005 shows the amino acid sequence (SEQ ID NO : 1005) derived from the coding sequence in Figure 1004.

Figure 1006A-B shows a nucleotide sequence (SEQ ID NO : 1006) of a native sequence PR050245 c. 1006 is a clone designated herein as "DNA255165".

Figure 1007 shows the amino acid sequence (SEQ ID NO : 1007) derived from the coding sequence in Figure 1006A-B.

Figure 1008 shows a nucleotide sequence (SEQ ID NO : 1008) of a native sequence PR083753 cDN. 1008 is a clone designated herein as "DNA327789".

Figure 1009 shows the amino acid sequence (SEQ ID NO : 1009) derived from the coding sequence in Figure 1008.

Figure 1010 shows a nucleotide sequence (SEQ ID NO : 1010) of a native sequence PRO83754 cDN,  
1010 is a clone designated herein as "DNA327790".

Figure 1011 shows the amino acid sequence (SEQ ID NO : 1011) derived from the coding sequence,  
in Figure 1010.

Figure 1012A-B shows a nucleotide sequence (SEQ ID NO : 1012) of a native sequence PRO83755 cDN,  
1012 is a clone designated herein as "DNA327791".

Figure 1013 shows the amino acid sequence (SEQ ID NO : 1013) derived from the coding sequence,  
in Figure 1012A-B.

Figure 1014A-B shows a nucleotide sequence (SEQ ID NO : 1014) of a native sequence PRO 83756  
is a clone designated herein as "DNA327792".

Figure 1015 shows the amino acid sequence (SEQ ID NO : 1015) derived from the coding sequence,  
in Figure 1014A-B.

Figure 1016 shows a nucleotide sequence (SEQ ID NO : 1016) of a native sequence PRO83757 cDN  
1016 is a clone designated herein as "DNA327793".

Figure 1017 shows the amino acid sequence (SEQ ID NO : 1017) derived from the coding sequence,  
in Figure 1016.

Figure 1018A-D shows a nucleotide sequence (SEQ ID NO : 1018) of a native sequence PRO83758 cDN,  
1018 is a clone designated herein as "DNA327794".

Figure 1019 shows the amino acid sequence (SEQ ID NO : 1019) derived from the coding sequence,  
in Figure 1018A-D.

Figure 1020 shows a nucleotide sequence (SEQ ID NO : 1020) of a native sequence cDNA, wherein :  
designated herein as "DNA327795".

Figure 1021 shows a nucleotide sequence (SEQ ID NO : 1021) of a native sequence PRO83760 cDN,  
1021 is a clone designated herein as "DNA327796".

Figure 1022 shows the amino acid sequence (SEQ ID NO : 1022) derived from the coding sequence,  
in Figure 1021.

Figure 1023 shows a nucleotide sequence (SEQ ID NO : 1023) of a native sequence PRO83761 cDN  
1023 is a clone designated herein as "DNA327797".

Figure 1024 shows the amino acid sequence (SEQ ID NO : 1024) derived from the coding sequence,  
in Figure 1023.

Figure 1025 shows a nucleotide sequence (SEQ ID NO : 1025) of a native sequence PRO83762 cDN,

1025 is a clone designated herein as "DNA327798".

Figure 1026 shows the amino acid sequence (SEQ ID NO : 1026) derived from the coding sequence in Figure 1025.

Figure 1027 shows a nucleotide sequence (SEQ ID NO : 1027) of a native sequence PR040011 cDN 1027 is a clone designated herein as "DNA327799".

Figure 1028 shows the amino acid sequence (SEQ ID NO : 1028) derived from the coding sequence in Figure 1027.

Figure 1029 shows a nucleotide sequence (SEQ ID NO : 1029) of a native sequence PR083763 cDN 1029 is a clone designated herein as "DNA327800".

Figure 1030 shows the amino acid sequence (SEQ ID NO : 1030) derived from the coding sequence in Figure 1029.

Figure 1031 shows a nucleotide sequence (SEQ ID NO : 1031) of a native sequence PRO11792 cDN 1031 is a clone designated herein as "DNA151422".

Figure 1032 shows the amino acid sequence (SEQ ID NO : 1032) derived from the coding sequence in Figure 1031.

Figure 1033 shows a nucleotide sequence (SEQ ID NO : 1033) of a native sequence PR083764 cDN 1033 is a clone designated herein as "DNA327801".

Figure 1034 shows the amino acid sequence (SEQ ID NO : 1034) derived from the coding sequence in Figure 1033.

Figure 1035 shows a nucleotide sequence (SEQ ID NO : 1035) of a native sequence PR071208 cDN 1035 is a clone designated herein as "DNA304796".

Figure 1036 shows the amino acid sequence (SEQ ID NO : 1036) derived from the coding sequence in Figure 1035.

Figure 1037 shows a nucleotide sequence (SEQ ID NO : 1037) of a native sequence PR083765 cDN 1037 is a clone designated herein as "DNA327802".

Figure 1038 shows the amino acid sequence (SEQ ID NO : 1083) derived from the coding sequence in Figure 1037.

Figure 1039A-B shows a nucleotide sequence (SEQ ID NO : 1039) of a native sequence PRO83766 1039 is a clone designated herein as "DNA327803".

Figure 1040 shows the amino acid sequence (SEQ ID NO : 1040) derived from the coding sequence in Figure 1039A-B.

Figure 1041 shows a nucleotide sequence (SEQ ID NO : 1041) of a native sequence PRO61547 cDN, 1041 is a clone designated herein as "DNA273569".

Figure 1042 shows the amino acid sequence (SEQ ID NO : 1042) derived from the coding sequence ( ) in Figure 1041.

Figure 1043 shows a nucleotide sequence (SEQ ID NO : 1043) of a native sequence PRO69493 cDN, 1043 is a clone designated herein as "DNA327804".

Figure 1044 shows the amino acid sequence (SEQ ID NO : 1044) derived from the coding sequence ( ) in Figure 1043.

Figure 1045 shows a nucleotide sequence (SEQ ID NO : 1045) of a native sequence cDNA, wherein : designated herein as "DNA327805".

Figure 1046 shows a nucleotide sequence (SEQ ID NO : 1046) of a native sequence PRO83767 cDN 1046 is a clone designated herein as "DNA327806".

Figure 1047 shows the amino acid sequence (SEQ ID NO : 1047) derived from the coding sequence ( ) in Figure 1046.

Figure 1048 shows a nucleotide sequence (SEQ ID NO : 1048) of a native sequence PRO83768 cDN 1048 is a clone designated herein as "DNA327807".

Figure 1049 shows the amino acid sequence (SEQ ID NO : 1049) derived from the coding sequence ( ) in Figure 1048.

Figure 1050 shows a nucleotide sequence (SEQ ID NO : 1050) of a native sequence PRO83769 cDN, 1050 is a clone designated herein as "DNA327808".

Figure 1051 shows the amino acid sequence (SEQ ID NO : 1051) derived from the coding sequence ( ) in Figure 1050.

Figure 1052 shows a nucleotide sequence (SEQ ID NO : 1052) of a native sequence PRO83770 cDN 1052 is a clone designated herein as "DNA327809".

Figure 1053 shows the amino acid sequence (SEQ ID NO : 1053) derived from the coding sequence ( ) in Figure 1052.

Figure 1054A-C shows a nucleotide sequence (SEQ ID NO : 1054) of a native sequence PRO12903 ( 1054 is a clone designated herein as "DNA151840".

Figure 1055 shows the amino acid sequence (SEQ ID NO1055 : ) derived from the coding sequence ( ) in Figure 1054A-C.

Figure 1056 shows a nucleotide sequence (SEQ ID NO : 1056) of a native sequence PRO83771 cDN,

1056 is a clone designated herein as "DNA327810".

Figure 1057 shows the amino acid sequence (SEQ ID NO : 1057) derived from the coding sequence in Figure 1056.

Figure 1058A-B shows a nucleotide sequence (SEQ ID NO : 1058) of a native sequence cDNA, where clone designated herein as "DNA256455".

Figure 1059 shows a nucleotide sequence (SEQ ID NO : 1059) of a native sequence PRO83772 cDN, 1059 is a clone designated herein as "DNA327811".

Figure 1060 shows the amino acid sequence (SEQ ID NO : 1060) derived from the coding sequence in Figure 1059.

Figure 1061 shows a nucleotide sequence (SEQ ID NO : 1061) of a native sequence PR049268 cDN, 1061 is a clone designated herein as "DNA254153".

Figure 1062 shows the amino acid sequence (SEQ ID NO : 1062) derived from the coding sequence in Figure 1061.

Figure 1063 shows a nucleotide sequence (SEQ ID NO : 1063) of a native sequence PRO83773 cDN, 1063 is a clone designated herein as "DNA327812".

Figure 1064 shows the amino acid sequence (SEQ ID NO : 1064) derived from the coding sequence in Figure 1063.

Figure 1065 shows a nucleotide sequence (SEQ ID NO : 1065) of a native sequence PRO83774 cDN, 1065 is a clone designated herein as "DNA327813".

Figure 1066 shows the amino acid sequence (SEQ ID NO : 1066) derived from the coding sequence in Figure 1065.

Figure 1067 shows a nucleotide sequence (SEQ ID NO : 1067) of a native sequence PR038184 cDN, 1067 is a clone designated herein as "DNA227721".

Figure 1068 shows the amino acid sequence (SEQ ID NO : 1068) derived from the coding sequence in Figure 1067.

Figure 1069 shows a nucleotide sequence (SEQ ID NO : 1069) of a native sequence PR071203 cDN, 1069 is a clone designated herein as "DNA304791".

Figure 1070 shows the amino acid sequence (SEQ ID NO : 1070) derived from the coding sequence in Figure 1069.

Figure 1071 shows a nucleotide sequence (SEQ ID NO : 1071) of a native sequence PR058654 cDN, 1071 is a clone designated herein as "DNA270266".



Figure 1072 shows the amino acid sequence (SEQ ID NO : 1072) derived from the coding sequence in Figure 1071.

Figure 1073 shows a nucleotide sequence (SEQ ID NO : 1073) of a native sequence PR02038 cDNA is a clone designated herein as "DNA327814".

Figure 1074 shows the amino acid sequence (SEQ ID NO : 1074) derived from the coding sequence in Figure 1073.

Figure 1075 shows a nucleotide sequence (SEQ ID NO : 1075) of a native sequence PR061547 cDNA 1075 is a clone designated herein as "DNA327815".

Figure 1076 shows the amino acid sequence (SEQ ID NO : 1076) derived from the coding sequence in Figure 1075.

Figure 1077 shows a nucleotide sequence (SEQ ID NO : 1077) of a native sequence PR082146 cDNA 1077 is a clone designated herein as "DNA327816".

Figure 1078 shows the amino acid sequence (SEQ ID NO : 1078) derived from the coding sequence in Figure 1077.

Figure 1079 shows a nucleotide sequence (SEQ ID NO : 1079) of a native sequence PRO868 cDNA is a clone designated herein as "DNA324728".

Figure 1080 shows the amino acid sequence (SEQ ID NO : 1080) derived from the coding sequence in Figure 1079.

Figure 1081A-B shows a nucleotide sequence (SEQ ID NO : 1081) of a native sequence PR02386 1081 is a clone designated herein as "DNA194507".

Figure 1082 shows the amino acid sequence (SEQ ID NO : 1082) derived from the coding sequence in Figure 1081A-B.

Figure 1083 shows a nucleotide sequence (SEQ ID NO : 1083) of a native sequence PRO1573 cDNA 1083 is a clone designated herein as "DNA327817".

Figure 1084 shows the amino acid sequence (SEQ ID NO : 1084) derived from the coding sequence in Figure 1083.

Figure 1085 shows a nucleotide sequence (SEQ ID NO : 1085) of a native sequence PR083775 cDNA 1085 is a clone designated herein as "DNA327818".

Figure 1086 shows the amino acid sequence (SEQ ID NO : 1086) derived from the coding sequence in Figure 1085.

Figure 1087 shows a nucleotide sequence (SEQ ID NO : 1087) of a native sequence cDNA where

designated herein as "DNA327819".

Figure 1088 shows a nucleotide sequence (SEQ ID NO : 1088) of a native sequence PR083776 cDNA, 1088 is a clone designated herein as "DNA327820".

Figure 1089 shows the amino acid sequence (SEQ ID NO : 1089) derived from the coding sequence in Figure 1088.

Figure 1090A-B shows a nucleotide sequence (SEQ ID NO : 1090) of a native sequence PR083777 cDNA, 1090 is a clone designated herein as "DNA327821".

Figure 1091 shows the amino acid sequence (SEQ ID NO : 1091) derived from the coding sequence in Figure 1090A-B.

Figure 1092 shows a nucleotide sequence (SEQ ID NO : 1092) of a native sequence PR04676 cDNA is a clone designated herein as "DNA288259".

Figure 1093 shows the amino acid sequence (SEQ ID NO : 1093) derived from the coding sequence in Figure 1092.

Figure 1094 shows a nucleotide sequence (SEQ ID NO : 1094) of a native sequence cDNA, wherein designated herein as "DNA271990".

Figure 1095A-B shows a nucleotide sequence (SEQ ID NO : 1095) of a native sequence cDNA, wherein clone designated herein as "DNA273734".

Figure 1096 shows a nucleotide sequence (SEQ ID NO : 1096) of a native sequence cDNA, wherein designated herein as "DNA327822".

Figure 1097 shows a nucleotide sequence (SEQ ID NO : 1097) of a native sequence PR083778 cDNA, 1097 is a clone designated herein as "DNA327823".

Figure 1098 shows the amino acid sequence (SEQ ID NO : 1098) derived from the coding sequence in Figure 1097.

Figure 1099A-B shows a nucleotide sequence (SEQ ID NO : 1099) of a native sequence PRO34518 cDNA, 1099 is a clone designated herein as "DNA327824".

Figure 1100 shows the amino acid sequence (SEQ ID NO : 1100) derived from the coding sequence in Figure 1099A-B.

Figure 1101 shows a nucleotide sequence (SEQ ID NO : 1101) of a native sequence cDNA, wherein designated herein as "DNA271933".

Figure 1102A-B shows a nucleotide sequence (SEQ ID NO : 1102) of a native sequence PR083779 cDNA, 1102 is a clone designated herein as "DNA327825".

Figure 1103 shows the amino acid sequence (SEQ ID NO : 1103) derived from the coding sequence in Figure 1102A-B.

Figure 1104A-B shows a nucleotide sequence (SEQ ID NO : 1104) of a native sequence PR024039 1104 is a clone designated herein as "DNA327826".

Figure 1105 shows the amino acid sequence (SEQ ID NO : 1105) derived from the coding sequence in Figure 1104A-B.

Figure 1106 shows a nucleotide sequence (SEQ ID NO : 1106) of a native sequence PR038060 cDN 1106 is a clone designated herein as "DNA227597".

Figure 1107 shows the amino acid sequence (SEQ ID NO : 1107) derived from the coding sequence in Figure 1106.

Figure 1108A-B shows a nucleotide sequence (SEQ ID NO : 1108) of a native sequence cDNA, whe clone designated herein as "DNA327827".

Figure 1109 shows a nucleotide sequence (SEQ ID NO : 1109) of a native sequence PR083780 cDN 1109 is a clone designated herein as "DNA327828".

Figure 1110 shows the amino acid sequence (SEQ ID NO : 1110) derived from the coding sequence in Figure 1109.

Figure 1111 shows a nucleotide sequence (SEQ ID NO : 1111) of a native sequence PR083781 cDN 1111 is a clone designated herein as "DNA327829".

Figure 1112 shows the amino acid sequence (SEQ ID NO : 1112) derived from the coding sequence in Figure 1111.

Figure 1113 shows a nucleotide sequence (SEQ ID NO : 1113) of a native sequence PR083782 cDN 1113 is a clone designated herein as "DNA327830".

Figure 1114 shows the amino acid sequence (SEQ ID NO : 1114) derived from the coding sequence in Figure 1113.

Figure 1115 shows a nucleotide sequence (SEQ ID NO : 1115) of a native sequence PRO83783 cDf 1115 is a clone designated herein as "DNA327831".

Figure 1116 shows the amino acid sequence (SEQ ID NO : 1116) derived from the coding sequence in Figure 1115.

Figure 1117 shows a nucleotide sequence (SEQ ID NO : 1117) of a native sequence PR083784 cDN 1117 is a clone designated herein as "DNA327832".

Figure 1118 shows the amino acid sequence (SEQ ID NO : 1118) derived from the coding sequence

in Figure 1117.

Figure 1119 shows a nucleotide sequence (SEQ ID NO : 1119) of a native sequence PR023628 cDN, 1119 is a clone designated herein as "DNA327833".

Figure 1120 shows the amino acid sequence (SEQ ID NO : 1120) derived from the coding sequence, in Figure 1119.

Figure 1121A-B shows a nucleotide sequence (SEQ ID NO : 1121) of a native sequence PRO83785, 1121 is a clone designated herein as "DNA327834".

Figure 1122 shows the amino acid sequence (SEQ ID NO : 1122) derived from the coding sequence, in Figure 1121A-B.

Figure 1123A-B shows a nucleotide sequence (SEQ ID NO : 1123) of a native sequence PRO83786, 1123 is a clone designated herein as "DNA327835".

Figure 1124 shows the amino acid sequence (SEQ ID NO : 1124) derived from the coding sequence, in Figure 1123A-B.

Figure 1125 shows a nucleotide sequence (SEQ ID NO : 1125) of a native sequence PR052581 cDN, 1125 is a clone designated herein as "DNA258641".

Figure 1126 shows the amino acid sequence (SEQ ID NO : 1126) derived from the coding sequence, in Figure 1125.

Figure 1127 shows a nucleotide sequence (SEQ ID NO : 1127) of a native sequence PR083787 cDN, 1127 is a clone designated herein as "DNA327836".

Figure 1128 shows the amino acid sequence (SEQ ID NO : 1128) derived from the coding sequence, in Figure 1127.

Figure 1129A-B shows a nucleotide sequence (SEQ ID NO : 1129) of a native sequence PR049486 c, 1129 is a clone designated herein as "DNA254376".

Figure 1130 shows the amino acid sequence (SEQ ID NO : 1130) derived from the coding sequence, in Figure 1129A-B.

Figure 1131 shows a nucleotide sequence (SEQ ID NO : 1131) of a native sequence PR083788 cDN, 1131 is a clone designated herein as "DNA327837".

Figure 1132 shows the amino acid sequence (SEQ ID NO : 1132) derived from the coding sequence, in Figure 1131.

Figure 1133 shows a nucleotide sequence (SEQ ID NO : 1133) of a native sequence PRO83789 cDN, 1133 is a clone designated herein as "DNA327838".

Figure 1134 shows the amino acid sequence (SEQ ID NO : 1134) derived from the coding sequence in Figure 1133.

Figure 1135 shows a nucleotide sequence (SEQ ID NO : 1135) of a native sequence PR038220 cDN 1135 is a clone designated herein as "DNA227757".

Figure 1136 shows the amino acid sequence (SEQ ID NO : 1136) derived from the coding sequence in Figure 1135.

Figure 1137 shows a nucleotide sequence (SEQ ID NO : 1137) of a native sequence PR02730 cDNA is a clone designated herein as "DNA88292".

Figure 1138 shows the amino acid sequence (SEQ ID NO : 1138) derived from the coding sequence ( in Figure 1137.

Figure 1139 shows a nucleotide sequence (SEQ ID NO : 1139) of a native sequence PR021884 cDN 139 is a clone designated herein as "DNA188349".

Figure 1140 shows the amino acid sequence (SEQ ID NO : 1140) derived from the coding sequence in Figure 1139.

Figure 1141 shows a nucleotide sequence (SEQ ID NO : 1141) of a native sequence PR083790 cDN 1141 is a clone designated herein as "DNA327839".

Figure 1142 shows the amino acid sequence (SEQ ID NO: 1142) derived from the coding sequence ( in Figure 1141.

Figure 1143 shows a nucleotide sequence (SEQ ID NO : 1143) of a native sequence PR037826 cDN 1143 is a clone designated herein as "DNA327840".

Figure 1144 shows the amino acid sequence (SEQ ID NO : 1144) derived from the coding sequence in Figure 1143.

Figure 1145 shows a nucleotide sequence (SEQ ID NO : 1145) of a native sequence PR058102 cDN 1145 is a clone designated herein as "DNA269692".

Figure 1146 shows the amino acid sequence (SEQ ID NO : 1146) derived from the coding sequence in Figure 1145, Figure 1147 shows a nucleotide sequence (SEQ ID NO : 1147) of a native sequence SEQ ID NO : 1147 is a clone designated herein as "DNA327841".

Figure 1148 shows the amino acid sequence (SEQ ID NO : 1148) derived from the coding sequence in Figure 1147.

Figure 1149 shows a nucleotide sequence (SEQ ID NO : 1149) of a native sequence PRO36639 cDN 1149 is a clone designated herein as "DNA226176".

Figure 1150 shows the amino acid sequence (SEQ ID NO : 1150) derived from the coding sequence in Figure 1149.

Figure 1151 shows a nucleotide sequence (SEQ ID NO : 1151) of a native sequence cDNA, wherein designated herein as "DNA195995".

Figure 1152 shows a nucleotide sequence (SEQ ID NO : 1152) of a native sequence PRO83791 cDNA 1152 is a clone designated herein as "DNA327842".

Figure 1153 shows the amino acid sequence (SEQ ID NO : 1153) derived from the coding sequence in Figure 1152.

Figure 1154 shows a nucleotide sequence (SEQ ID NO : 1154) of a native sequence PRO81472 cDNA 1154 is a clone designated herein as "DNA327843".

Figure 1155 shows the amino acid sequence (SEQ ID NO : 1155) derived from the coding sequence c in Figure 1154.

Figure 1156 shows a nucleotide sequence (SEQ ID NO : 1156) of a native sequence PR051365 cDNA 1156 is a clone designated herein as "DNA327844".

Figure 1157 shows the amino acid sequence (SEQ ID NO : 1157) derived from the coding sequence in Figure 1156.

Figure 1158 shows a nucleotide sequence (SEQ ID NO : 1158) of a native sequence PR069463 cDNA 1158 is a clone designated herein as "DNA287173".

Figure 1159 shows the amino acid sequence (SEQ ID NO : 1159) derived from the coding sequence in Figure 1158.

Figure 1160 shows a nucleotide sequence (SEQ ID NO : 1160) of a native sequence PR061271 cDNA 1160 is a clone designated herein as "DNA327845".

Figure 1161 shows the amino acid sequence (SEQ ID NO : 1161) derived from the coding sequence in Figure 1160.

Figure 1162 shows a nucleotide sequence (SEQ ID NO : 1162) of a native sequence cDNA, wherein designated herein as "DNA196182".

Figure 1163 shows a nucleotide sequence (SEQ ID NO : 1163) of a native sequence PRO83792 cDNA 1163 is a clone designated herein as "DNA327846".

Figure 1164 shows the amino acid sequence (SEQ ID NO : 1164) derived from the coding sequence in Figure 1163.

Figure 1165A-B shows a nucleotide sequence (SEQ ID NO : 1165) of a native sequence PR02834 cDNA 1165 is a clone designated herein as "DNA327847".

Figure 1166 shows the amino acid sequence (SEQ ID NO : 1166) derived from the coding sequence in Figure 1165A-B.

Figure 1167 shows a nucleotide sequence (SEQ ID NO : 1167) of a native sequence PR02834 cDNA is a clone designated herein as "DNA88541".

Figure 1168 shows the amino acid sequence (SEQ ID NO : 1168) derived from the coding sequence in Figure 1167.

Figure 1169 shows a nucleotide sequence (SEQ ID NO : 1169) of a native sequence PR083793 cDNA is a clone designated herein as "DNA327848".

Figure 1170 shows the amino acid sequence (SEQ ID NO : 1170) derived from the coding sequence in Figure 1169.

Figure 1171 shows a nucleotide sequence (SEQ ID NO : 1171) of a native sequence PR083794 cDNA 1171 is a clone designated herein as "DNA327849".

Figure 1172 shows the amino acid sequence (SEQ ID NO : 1172) derived from the coding sequence in Figure 1171.

Figure 1173A-B shows a nucleotide sequence (SEQ ID NO : 1173) of a native sequence PR02237 1173 is a clone designated herein as "DNA88226".

Figure 1174 shows the amino acid sequence (SEQ ID NO : 1174) derived from the coding sequence in Figure 1173A-B.

Figure 1175 shows a nucleotide sequence (SEQ ID NO : 1175) of a native sequence PR060803 cDNA 1175 is a clone designated herein as "DNA327850".

Figure 1176 shows the amino acid sequence (SEQ ID NO : 1176) derived from the coding sequence in Figure 1175.

Figure 1177 shows a nucleotide sequence (SEQ ID NO : 1177) of a native sequence PR080741 cDNA 1177 is a clone designated herein as "DNA324022".

Figure 1178 shows the amino acid sequence (SEQ ID NO : 1178) derived from the coding sequence in Figure 1177.

Figure 1179 shows a nucleotide sequence (SEQ ID NO : 1179) of a native sequence PR083795 cDNA 1179 is a clone designated herein as "DNA327851".

Figure 1180 shows the amino acid sequence (SEQ ID NO : 1180) derived from the coding sequence in Figure 1179.

Figure 1181 shows a nucleotide sequence (SEQ ID NO : 1181) of a native sequence PR060759 cDN, 1181 is a clone designated herein as "DNA272626".

Figure 1182 shows the amino acid sequence (SEQ ID NO : 1182) derived from the coding sequence ( in Figure 1181.

Figure 1183 shows a nucleotide sequence (SEQ ID NO : 1183) of a native sequence PR037222 cDN, 1183 is a clone designated herein as "DNA226759".

Figure 1184 shows the amino acid sequence (SEQ ID NO : 1184) derived from the coding sequence ( in Figure 1183.

Figure 1185A-B shows a nucleotide sequence (SEQ ID NO : 1185) of a native sequence PR081523 c 1185 is a clone designated herein as "DNA324921".

Figure 1186 shows the amino acid sequence (SEQ ID NO : 1186) derived from the coding sequence ( in Figure 1185A-B.

Figure 1187 shows a nucleotide sequence (SEQ ID NO : 1187) of a native sequence PR083796 cDN, 1187 is a clone designated herein as "DNA327852".

Figure 1188 shows the amino acid sequence (SEQ ID NO : 1188) derived from the coding sequence ( in Figure 1187.

Figure 1189 shows a nucleotide sequence (SEQ ID NO : 1189) of a native sequence PR082223 cDN, 1189 is a clone designated herein as "DNA327853".

Figure 1190 shows the amino acid sequence (SEQ ID NO : 1190) derived from the coding sequence ( in Figure 1189.

Figure 1191A-B shows a nucleotide sequence (SEQ ID NO : 1191) of a native sequence PR083797 c 1191 is a clone designated herein as "DNA327854".

Figure 1192 shows the amino acid sequence (SEQ ID NO : 1192) derived from the coding sequence ( in Figure 1191A-B.

Figure 1193 shows a nucleotide sequence (SEQ ID NO : 1193) of a native sequence PR083367 cDN, 1193 is a clone designated herein as "DNA327855".

Figure 1194 shows the amino acid sequence (SEQ ID NO : 1194) derived from the coding sequence ( in Figure 1193.

Figure 1195 shows a nucleotide sequence (SEQ ID NO : 1195) of a native sequence PR061079 cDN, 1195 is a clone designated herein as "DNA273008".

Figure 1196 shows the amino acid sequence (SEQ ID NO : 1196) derived from the coding sequence ( in Figure 1195.



Figure 1197A-B shows a nucleotide sequence (SEQ ID NO : 1197) of a native sequence PR083798 1197 is a clone designated herein as "DNA327856".

Figure 1198 shows the amino acid sequence (SEQ ID NO : 1198) derived from the coding sequence in Figure 1197A-B.

Figure 1199 shows a nucleotide sequence (SEQ ID NO : 1199) of a native sequence PR037776 cDNA 1199 is a clone designated herein as "DNA227313".

Figure 1200 shows the amino acid sequence (SEQ ID NO : 1200) derived from the coding sequence in Figure 1199.

Figure 1201 shows a nucleotide sequence (SEQ ID NO : 1201) of a native sequence PR037961 cDNA 1201 is a clone designated herein as "DNA227498".

Figure 1202 shows the amino acid sequence (SEQ ID NO : 1202) derived from the coding sequence in Figure 1201.

Figure 1203 shows a nucleotide sequence (SEQ ID NO : 1203) of a native sequence PR083799 cDNA 1203 is a clone designated herein as "DNA327857".

Figure 1204 shows the amino acid sequence (SEQ ID NO : 1204) derived from the coding sequence in Figure 1203.

Figure 1205 shows a nucleotide sequence (SEQ ID NO : 1205) of a native sequence PR049837 cDNA 1205 is a clone designated herein as "DNA254739".

Figure 1206 shows the amino acid sequence (SEQ ID NO : 1206) derived from the coding sequence in Figure 1205.

Figure 1207 shows a nucleotide sequence (SEQ ID NO : 1207) of a native sequence PR083800 cDNA 1207 is a clone designated herein as "DNA327858".

Figure 1208 shows the amino acid sequence (SEQ ID NO : 1208) derived from the coding sequence in Figure 1207.

Figure 1209 shows a nucleotide sequence (SEQ ID NO : 1209) of a native sequence PR069677 cDNA 1209 is a clone designated herein as "DNA287420".

Figure 1210 shows the amino acid sequence (SEQ ID NO : 1210) derived from the coding sequence in Figure 1209.

Figure 1211 shows a nucleotide sequence (SEQ ID NO : 1211) of a native sequence PR037748 cDNA 1211 is a clone designated herein as "DNA327859".

Figure 1212 shows the amino acid sequence (SEQ ID NO : 1212) derived from the coding sequence in Figure 1211.

Figure 1213 shows a nucleotide sequence (SEQ ID NO : 1213) of a native sequence PRO83801 1213 is a clone designated herein as "DNA327860".

Figure 1214 shows the amino acid sequence (SEQ ID NO : 1214) derived from the coding sequence in Figure 1213.

Figure 1215 shows a nucleotide sequence (SEQ ID NO : 1215) of a native sequence PRO83802 , 1215 is a clone designated herein as "DNA327861".

Figure 1216 shows the amino acid sequence (SEQ ID NO : 1216) derived from the coding sequence in Figure 1215.

Figure 1217 shows a nucleotide sequence (SEQ ID NO : 1217) of a native sequence PRO83803 , 1217 is a clone designated herein as "DNA327862".

Figure 1218 shows the amino acid sequence (SEQ ID NO : 1218) derived from the coding sequence in Figure 1217.

Figure 1219 shows a nucleotide sequence (SEQ ID NO : 1219) of a native sequence PRO83804 , 1219 is a clone designated herein as "DNA327863".

Figure 1220 shows the amino acid sequence (SEQ ID NO : 1220) derived from the coding sequence in Figure 1219.

Figure 1221 shows a nucleotide sequence (SEQ ID NO : 1221) of a native sequence PRO50409 1221 is a clone designated herein as "DNA255340".

Figure 1222 shows the amino acid sequence (SEQ ID NO : 1222) derived from the coding sequence in Figure 1221.

Figure 1223A-B shows a nucleotide sequence (SEQ ID NO : 1223) of a native sequence PRO694 1223 is a clone designated herein as "DNA287192".

Figure 1224 shows the amino acid sequence (SEQ ID NO : 1224) derived from the coding sequence in Figure 1223A-B.

Figure 1225 shows a nucleotide sequence (SEQ ID NO : 1225) of a native sequence PRO83805 1225 is a clone designated herein as "DNA327864".

Figure 1226 shows the amino acid sequence (SEQ ID NO : 1226) derived from the coding sequence in Figure 1225.

Figure 1227 shows a nucleotide sequence (SEQ ID NO : 1227) of a native sequence PRO83806 1227 is a clone designated herein as "DNA 327865".

Figure 1228 shows the amino acid sequence (SEQ ID NO : 1228) derived from the coding sequence in Figure 1227.

Figure 1229 shows a nucleotide sequence (SEQ ID NO : 1229) of a native sequence PR083807 cDN 1229 is a clone designated herein as "DNA327866".

Figure 1230 shows the amino acid sequence (SEQ ID NO : 1230) derived from the coding sequence in Figure 1229.

Figure 1231 shows a nucleotide sequence (SEQ ID NO : 1231) of a native sequence PR083808 cDN 1231 is a clone designated herein as "DNA327867".

Figure 1232 shows the amino acid sequence (SEQ ID NO : 1232) derived from the coding sequence in Figure 1231.

Figure 1233 shows a nucleotide sequence (SEQ ID NO : 1233) of a native sequence PR083809 cDN 1233 is a clone designated herein as "DNA327868".

Figure 1234 shows the amino acid sequence (SEQ ID NO : 1234) derived from the coding sequence in Figure 1233.

Figure 1235 shows a nucleotide sequence (SEQ ID NO : 1235) of a native sequence PRO1898 cDN/ 1235 is a clone designated herein as "DNA327869".

Figure 1236 shows the amino acid sequence (SEQ ID NO : 1236) derived from the coding sequence in Figure 1235.

Figure 1237 shows a nucleotide sequence (SEQ ID NO : 1237) of a native sequence PRO83810 cDN 1237 is a clone designated herein as "DNA327870".

Figure 1238 shows the amino acid sequence (SEQ ID NO : 1238) derived from the coding sequence in Figure 1237.

Figure 1239 shows a nucleotide sequence (SEQ ID NO : 1239) of a native sequence PR060668 cDN 1239 is a clone designated herein as "DNA272415".

Figure 1240 shows the amino acid sequence (SEQ ID NO : 1240) derived from the coding sequence in Figure 1239.

Figure 1241 shows a nucleotide sequence (SEQ ID NO : 1241) of a native sequence PR037056 cDN 1241 is a clone designated herein as "DNA226593".

Figure 1242 shows the amino acid sequence (SEQ ID NO : 1242) derived from the coding sequence in Figure 1241.

Figure 1243 shows a nucleotide sequence (SEQ ID NO : 1243) of a native sequence PRO83811 1243 is a clone designated herein as "DNA327871".

Figure 1244 shows the amino acid sequence (SEQ ID NO : 1244) derived from the coding sequence in Figure 1243.

Figure 1245 shows a nucleotide sequence (SEQ ID NO : 1245) of a native sequence PR050616 , 1245 is a clone designated herein as "DNA25552".

Figure 1246 shows the amino acid sequence (SEQ ID NO : 1246) derived from the coding sequence in Figure 1245.

Figure 1247 shows a nucleotide sequence (SEQ ID NO : 1247) of a native sequence PRO83812 1247 is a clone designated herein as "DNA327872".

Figure 1248 shows the amino acid sequence (SEQ ID NO : 1248) derived from the coding sequence in Figure 1247.

Figure 1249 shows a nucleotide sequence (SEQ ID NO : 1249) of a native sequence PRO83813 1249 is a clone designated herein as "DNA327873".

Figure 1250 shows the amino acid sequence (SEQ ID NO : 1250) derived from the coding sequence in Figure 1249.

Figure 1251 shows a nucleotide sequence (SEQ ID NO : 1251) of a native sequence PRO4805 c 1251 is a clone designated herein as "DNA327874".

Figure 1252 shows the amino acid sequence (SEQ ID NO : 1252) derived from the coding sequence in Figure 1251.

Figure 1253 shows a nucleotide sequence (SEQ ID NO : 1253) of a native sequence PRO69459 1253 is a clone designated herein as "DNA287166".

Figure 1254 shows the amino acid sequence (SEQ ID NO : 1254) derived from the coding sequence in Figure 1253.

Figure 1255 shows a nucleotide sequence (SEQ ID NO : 1255) of a native sequence PR083814 , 1255 is a clone designated herein as "DNA327875".

Figure 1256 shows the amino acid sequence (SEQ ID NO : 1256) derived from the coding sequence in Figure 1255.

Figure 1257 shows a nucleotide sequence (SEQ ID NO : 1257) of a native sequence PR066032 , 1257 is a clone designated herein as "DNA279661".

Figure 1258 shows the amino acid sequence (SEQ ID NO : 1258) derived from the coding sequence in Figure 1257.

Figure 1259 shows a nucleotide sequence (SEQ ID NO : 1259) of a native sequence PR051309 cDN, 1259 is a clone designated herein as "DNA256265".

Figure 1260 shows the amino acid sequence (SEQ ID NO : 1260) derived from the coding sequence, in Figure 1259.

Figure 1261 shows a nucleotide sequence (SEQ ID NO : 1216) of a native sequence PRO83469 cDN, 1261 is a clone designated herein as "DNA327191".

Figure 1262 shows the amino acid sequence (SEQ ID NO : 1262) derived from the coding sequence, in Figure 1261.

Figure 1263 shows a nucleotide sequence (SEQ ID NO : 1263) of a native sequence PRO83815 cDN, 1263 is a clone designated herein as "DNA327876".

Figure 1264 shows the amino acid sequence (SEQ ID NO : 1264) derived from the coding sequence, in Figure 1263.

Figure 1265 shows a nucleotide sequence (SEQ ID NO : 1265) of a native sequence PR083816 cDN, 1265 is a clone designated herein as "DNA327877".

Figure 1266 shows the amino acid sequence (SEQ ID NO : 1266) derived from the coding sequence, in Figure 1265.

Figure 1267 shows a nucleotide sequence (SEQ ID NO : 1267) of a native sequence PR034321 cDN, 1267 is a clone designated herein as "DNA218269".

Figure 1268 shows the amino acid sequence (SEQ ID NO : 1268) derived from the coding sequence, in Figure 1267.

Figure 1269 shows a nucleotide sequence (SEQ ID NO : 1269) of a native sequence PR070808 cDN, 1269 is a clone designated herein as "DNA297191".

Figure 1270 shows the amino acid sequence (SEQ ID NO : 1270) derived from the coding sequence, in Figure 1269.

Figure 1271 shows a nucleotide sequence (SEQ ID NO : 1271) of a native sequence PRO83817 cDN, 1271 is a clone designated herein as "DNA327878".

Figure 1272 shows the amino acid sequence (SEQ ID NO : 1272) derived from the coding sequence, in Figure 1271.

Figure 1273 shows a nucleotide sequence (SEQ ID NO : 1273) of a native sequence PR083818 cDN, 1273 is a clone designated herein as "DNA327879".

Figure 1274 shows the amino acid sequence (SEQ ID NO : 1274) derived from the coding sequence in Figure 1273.

Figure 1275 shows a nucleotide sequence (SEQ ID NO : 1275) of a native sequence PR083819 cDN 1275 is a clone designated herein as "DNA327880".

Figure 1276 shows the amino acid sequence (SEQ ID NO : 1276) derived from the coding sequence in Figure 1275.

Figure 1277 shows a nucleotide sequence (SEQ ID NO : 1277) of a native sequence PR083820 cDN 1277 is a clone designated herein as "DNA327881".

Figure 1278 shows the amino acid sequence (SEQ ID NO : 1278) derived from the coding sequence in Figure 1277.

Figure 1279 shows a nucleotide sequence (SEQ ID NO : 1279) of a native sequence PR031794 cDN 1279 is a clone designated herein as "DNA327882".

Figure 1280 shows the amino acid sequence (SEQ ID NO : 1280) derived from the coding sequence in Figure 1279.

Figure 1281 shows a nucleotide sequence (SEQ ID NO : 1281) of a native sequence PRO82421 cDN 1281 is a clone designated herein as "DNA325976".

Figure 1282 shows the amino acid sequence (SEQ ID NO : 1282) derived from the coding sequence in Figure 1281.

Figure 1283 shows a nucleotide sequence (SEQ ID NO : 1283) of a native sequence PR049810 cDN 1283 is a clone designated herein as "DNA254710".

Figure 1284 shows the amino acid sequence (SEQ ID NO : 1284) derived from the coding sequence in Figure 1283.

Figure 1285 shows a nucleotide sequence (SEQ ID NO : 1285) of a native sequence PR059776 cDN 1285 is a clone designated herein as "DNA271483".

Figure 1286 shows the amino acid sequence (SEQ ID NO : 1286) derived from the coding sequence in Figure 1285.

Figure 1287 shows a nucleotide sequence (SEQ ID NO : 1287) of a native sequence PR083821 cDN 1287 is a clone designated herein as "DNA327883".

Figure 1288 shows the amino acid sequence (SEQ ID NO : 1288) derived from the coding sequence in Figure 1287.

Figure 1289 shows a nucleotide sequence (SEQ ID NO : 1289) of a native sequence PRO83822 cDN 1289 is a clone designated herein as "DNA327884".

Figure 1290 shows the amino acid sequence (SEQ ID NO : 1290) derived from the coding sequence in Figure 1289.

Figure 1291 shows a nucleotide sequence (SEQ ID NO : 1291) of a native sequence PR082377 cDN 1291 is a clone designated herein as "DNA327885".

Figure 1292 shows the amino acid sequence (SEQ ID NO : 1292) derived from the coding sequence in Figure 1291.

Figure 1293 shows a nucleotide sequence (SEQ ID NO : 1293) of a native sequence PR041077 cDN 1293 is a clone designated herein as "DNA327886".

Figure 1294 shows the amino acid sequence (SEQ ID NO : 1294) derived from the coding sequence in Figure 1293.

Figure 1295 shows a nucleotide sequence (SEQ ID NO : 1295) of a native sequence PR083823 cDN 1295 is a clone designated herein as "DNA327887".

Figure 1296 shows the amino acid sequence (SEQ ID NO : 1296) derived from the coding sequence in Figure 1295.

Figure 1297 shows a nucleotide sequence (SEQ ID NO : 1297) of a native sequence PRO83824 cDN 1297 is a clone designated herein as "DNA327888".

Figure 1298 shows the amino acid sequence (SEQ ID NO : 1298) derived from the coding sequence in Figure 1297.

Figure 1299 shows a nucleotide sequence (SEQ ID NO : 1299) of a native sequence PRO83825 cDN 1299 is a clone designated herein as "DNA327889".

Figure 1300 shows the amino acid sequence (SEQ ID NO : 1300) derived from the coding sequence in Figure 1299.

Figure 1301 shows a nucleotide sequence (SEQ ID NO : 1301) of a native sequence PRO83826 cDN 1301 is a clone designated herein as "DNA327890".

Figure 1302 shows the amino acid sequence (SEQ ID NO : 1302) derived from the coding sequence in Figure 1301.

Figure 1303 shows a nucleotide sequence (SEQ ID NO : 1303) of a native sequence PR050546 cDN 1303 is a clone designated herein as "DNA255479".

Figure 1304 shows the amino acid sequence (SEQ ID NO : 1304) derived from the coding sequence in Figure 1303.

Figure 1305 shows a nucleotide sequence (SEQ ID NO : 1305) of a native sequence PRO83827 1305 is a clone designated herein as "DNA327891".

Figure 1306 shows the amino acid sequence (SEQ ID NO : 1306) derived from the coding sequence in Figure 1305.

Figure 1307 shows a nucleotide sequence (SEQ ID NO : 1307) of a native sequence PR037408 , 1307 is a clone designated herein as "DNA226945".

Figure 1308 shows the amino acid sequence (SEQ ID NO : 1308) derived from the coding sequence in Figure 1307.

Figure 1309 shows a nucleotide sequence (SEQ ID NO : 1309) of a native sequence PRO83828 1309 is a clone designated herein as "DNA327892".

Figure 1310 shows the amino acid sequence (SEQ ID NO : 1310) derived from the coding sequence in Figure 1309.

Figure 1311 shows a nucleotide sequence (SEQ ID NO : 1311) of a native sequence PRO83829 1311 is a clone designated herein as "DNA327893".

Figure 1312 shows the amino acid sequence (SEQ ID NO : 1312) derived from the coding sequence in Figure 1311.

Figure 1313 shows a nucleotide sequence (SEQ ID NO : 1313) of a native sequence PR050241 , 1313 is a clone designated herein as "DNA255161".

Figure 1314 shows the amino acid sequence (SEQ ID NO : 1314) derived from the coding sequence in Figure 1313.

Figure 1315 shows a nucleotide sequence (SEQ ID NO : 1315) of a native sequence PR037102 , 1315 is a clone designated herein as "DNA226639".

Figure 1316 shows the amino acid sequence (SEQ ID NO : 1316) derived from the coding sequence in Figure 1315.

Figure 1317 shows a nucleotide sequence (SEQ ID NO : 1317) of a native sequence PR069488 , 1317 is a clone designated herein as "DNA287206".

Figure 1318 shows the amino acid sequence (SEQ ID NO : 1318) derived from the coding sequence in Figure 1317.

Figure 1319 shows a nucleotide sequence (SEQ ID NO : 1319) of a native sequence PR083830 , 1319 is a clone designated herein as "DNA327894".

Figure 1320 shows the amino acid sequence (SEQ ID NO : 1320) derived from the coding sequence in Figure 1319.



Figure 1321 shows a nucleotide sequence (SEQ ID NO : 1321) of a native sequence PR083831 cDN,  
1321 is a clone designated herein as "DNA327896".

Figure 1322 shows the amino acid sequence (SEQ ID NO : 1322) derived from the coding sequence  
in Figure 1321.

Figure 1323 shows a nucleotide sequence (SEQ ID NO : 1323) of a native sequence PR083832 cDN  
1323 is a clone designated herein as "DNA327896".

Figure 1324 shows the amino acid sequence (SEQ ID NO : 1324) derived from the coding sequence  
in Figure 1323.

Figure 1325 shows a nucleotide sequence (SEQ ID NO : 1325) of a native sequence PR033675 cDN,  
1325 is a clone designated herein as "DNA210130".

Figure 1326 shows the amino acid sequence (SEQ ID NO : 1326) derived from the coding sequence  
in Figure 1325.

Figure 1327 shows a nucleotide sequence (SEQ ID NO : 1327) of a native sequence PR083833 cDN,  
1327 is a clone designated herein as "DNA327897".

Figure 1328 shows the amino acid sequence (SEQ ID NO : 1328) derived from the coding sequence  
in Figure 1327.

Figure 1329 shows a nucleotide sequence (SEQ ID NO : 1329) of a native sequence PR038467 cDN,  
1329 is a clone designated herein as "DNA228004".

Figure 1330 shows the amino acid sequence (SEQ ID NO : 1330) derived from the coding sequence  
in Figure 1329.

Figure 1331 shows a nucleotide sequence (SEQ ID NO : 1331) of a native sequence PR038250 cDN,  
1331 is a clone designated herein as "DNA227787".

Figure 1332 shows the amino acid sequence (SEQ ID NO : 1332) derived from the coding sequence  
in Figure 1331.

Figure 1333 shows a nucleotide sequence (SEQ ID NO : 1333) of a native sequence PR038854 cDN,  
1333 is a clone designated herein as "DNA327898".

Figure 1334 shows the amino acid sequence (SEQ ID NO : 1334) derived from the coding sequence  
in Figure 1333.

Figure 1335 shows a nucleotide sequence (SEQ ID NO : 1335) of a native sequence PR082424 cDN  
1335 is a clone designated herein as "DNA325979".

Figure 1336 shows the amino acid sequence (SEQ ID NO : 1336) derived from the coding sequence in Figure 1335.

Figure 1337 shows a nucleotide sequence (SEQ ID NO : 1337) of a native sequence PR083834 cDN is a clone designated herein as "DNA327899".

Figure 1338 shows the amino acid sequence (SEQ ID NO : 1338) derived from the coding sequence in Figure 1337.

Figure 1339 shows a nucleotide sequence (SEQ ID NO : 1339) of a native sequence PR051573 cDN 1339 is a clone designated herein as "DNA256541".

Figure 1340 shows the amino acid sequence (SEQ ID NO : 140) derived from the coding sequence c in Figure 1339.

Figure 1341 shows a nucleotide sequence (SEQ ID NO : 1341) of a native sequence PR034753 cDN 1341 is a clone designated herein as "DNA221079".

Figure 1342 shows the amino acid sequence (SEQ ID NO : 1342) derived from the coding sequence in Figure 1341.

Figure 1343 shows a nucleotide sequence (SEQ ID NO : 1343) of a native sequence PR083835 cDN 1343 is a clone designated herein as "DNA327900".

Figure 1344 shows the amino acid sequence (SEQ ID NO : 1344) derived from the coding sequence in Figure 1343.

Figure 1345 shows a nucleotide sequence (SEQ ID NO : 1345) of a native sequence PR083836 cDN 1345 is a clone designated herein as "DNA327901".

Figure 1346 shows the amino acid sequence (SEQ ID NO : 1346) derived from the coding sequence in Figure 1345.

Figure 1347 shows a nucleotide sequence (SEQ ID NO : 1347) of a native sequence PR083837 cDN 1347 is a clone designated herein as "DNA327902".

Figure 1348 shows the amino acid sequence (SEQ ID NO : 1348) derived from the coding sequence in Figure 1347.

Figure 1349 shows a nucleotide sequence (SEQ ID NO : 1349) of a native sequence PR083838 cDN 1349 is a clone designated herein as "DNA327903".

Figure 1350 shows the amino acid sequence (SEQ ID NO : 1350) derived from the coding sequence in Figure 1349.

Figure 1351 shows a nucleotide sequence (SEQ ID NO : 1351) of a native sequence PR083839 cDN 1351 is a clone designated herein as "DNA327904".

Figure 1352 shows the amino acid sequence (SEQ ID NO : 1352) derived from the coding sequence in Figure 1351.

Figure 1353 shows a nucleotide sequence (SEQ ID NO : 1353) of a native sequence PRO51567 of 1353 is a clone designated herein as "DNA256535".

Figure 1354 shows the amino acid sequence (SEQ ID NO : 1354) derived from the coding sequence in Figure 1353.

Figure 1355 shows a nucleotide sequence (SEQ ID NO : 1355) of a native sequence PR049407 of 1355 is a clone designated herein as "DNA254296".

Figure 1356 shows the amino acid sequence (SEQ ID NO : 1356) derived from the coding sequence in Figure 1355.

Figure 1357 shows a nucleotide sequence (SEQ ID NO : 1357) of a native sequence PR083840 of 1357 is a clone designated herein as "DNA327905".

Figure 1358 shows the amino acid sequence (SEQ ID NO : 1358) derived from the coding sequence in Figure 1357.

Figure 1359 shows a nucleotide sequence (SEQ ID NO : 1359) of a native sequence PRO51079 of 1359 is a clone designated herein as "DNA256031".

Figure 1360 shows the amino acid sequence (SEQ ID NO : 1360) derived from the coding sequence in Figure 1359.

Figure 1361 shows a nucleotide sequence (SEQ ID NO : 1361) of a native sequence PRO83841 of 1361 is a clone designated herein as "DNA327906".

Figure 1362 shows the amino acid sequence (SEQ ID NO : 1362) derived from the coding sequence in Figure 1361.

Figure 1363 shows a nucleotide sequence (SEQ ID NO : 1363) of a native sequence PR083842 of 1363 is a clone designated herein as "DNA327907".

Figure 1364 shows the amino acid sequence (SEQ ID NO : 1364) derived from the coding sequence in Figure 1363.

Figure 1365 shows a nucleotide sequence (SEQ ID NO : 1365) of a native sequence PR037831 of 1365 is a clone designated herein as "DNA227368".

Figure 1366 shows the amino acid sequence (SEQ ID NO : 1366) derived from the coding sequence in Figure 1365.

Figure 1367 shows a nucleotide sequence (SEQ ID NO : 1367) of a native sequence PR083843 cDN,  
1367 is a clone designated herein as "DNA327908".

Figure 1368 shows the amino acid sequence (SEQ ID NO : 1368) derived from the coding sequence,  
in Figure 1367.

Figure 1369 shows a nucleotide sequence (SEQ ID NO : 1369) of a native sequence PR083844 cDN,  
1369 is a clone designated herein as "DNA327909".

Figure 1370 shows the amino acid sequence (SEQ ID NO : 1370) derived from the coding sequence,  
in Figure 1369.

Figure 1371 shows a nucleotide sequence (SEQ ID NO : 1371) of a native sequence PR083845 cDN,  
1371 is a clone designated herein as "DNA327910".

Figure 1372 shows the amino acid sequence (SEQ ID NO : 1372) derived from the coding sequence,  
in Figure 1371.

Figure 1373 shows a nucleotide sequence (SEQ ID NO : 1373) of a native sequence PR083846 cDN,  
1373 is a clone designated herein as "DNA327911".

Figure 1374 shows the amino acid sequence (SEQ ID NO : 1374) derived from the coding sequence,  
in Figure 1373.

Figure 1375 shows a nucleotide sequence (SEQ ID NO : 1375) of a native sequence PR083847 cDN,  
1375 is a clone designated herein as "DNA327912".

Figure 1376 shows the amino acid sequence (SEQ ID NO : 1376) derived from the coding sequence,  
in Figure 1375.

Figure 1377 shows a nucleotide sequence (SEQ ID NO : 1377) of a native sequence PR083848 cDN,  
1377 is a clone designated herein as "DNA327913".

Figure 1378 shows the amino acid sequence (SEQ ID NO : 1378) derived from the coding sequence,  
in Figure 1377.

Figure 1379 shows a nucleotide sequence (SEQ ID NO : 1379) of a native sequence PR083849 cDN,  
1379 is a clone designated herein as "DNA327914".

Figure 1380 shows the amino acid sequence (SEQ ID NO : 1379) derived from the coding sequence,  
in Figure 1380.

Figure 1381 shows a nucleotide sequence (SEQ ID NO : 1381) of a native sequence PR050532 cDN,  
1381 is a clone designated herein as "DNA255465".

Figure 1382 shows the amino acid sequence (SEQ ID NO : 1382) derived from the coding sequence,  
in Figure 1381

Figure 1383 shows a nucleotide sequence (SEQ ID NO : 1383) of a native sequence PR083850 cDN, 1383 is a clone designated herein as "DNA327915".

Figure 1384 shows the amino acid sequence (SEQ ID NO : 1384) derived from the coding sequence , in Figure 1383.

Figure 1385 shows a nucleotide sequence (SEQ ID NO : 1385) of a native sequence PR050821 cDN, 1385 is a clone designated herein as "DNA255766".

Figure 1386 shows the amino acid sequence (SEQ ID NO : 1386) derived from the coding sequence , in Figure.

Figure 1387 shows a nucleotide sequence (SEQ ID NO : 1387) of a native sequence PR070011 cDN, 1387 is a clone designated herein as "DNA288247".

Figure 1388 shows the amino acid sequence (SEQ ID NO : 1388) derived from the coding sequence , in Figure 1387.

Figure 1389 shows a nucleotide sequence (SEQ ID NO : 1389) of a native sequence PR083851 cDN, 1389 is a clone designated herein as "DNA327916".

Figure 1390 shows the amino acid sequence (SEQ ID NO : 1390) derived from the coding sequence , in Figure 1389.

Figure 1391 shows a nucleotide sequence (SEQ ID NO : 1391) of a native sequence PR083852 cDN, 1391 is a clone designated herein as "DNA327917".

Figure 1392 shows the amino acid sequence (SEQ ID NO : 1392) derived from the coding sequence , in Figure 1391.

Figure 1393 shows a nucleotide sequence (SEQ ID NO : 1393) of a native sequence PR083853 cDN, 1393 is a clone designated herein as "DNA327918".

Figure 1394 shows the amino acid sequence (SEQ ID NO : 1394) derived from the coding sequence , in Figure 1393.

Figure 1395 shows a nucleotide sequence (SEQ ID NO : 1395) of a native sequence PRO83854 cDN 1395 is a clone designated herein as "DNA327919".

Figure 1396 shows the amino acid sequence (SEQ ID NO : 1396) derived from the coding sequence , in Figure 1395.

Figure 1397 shows a nucleotide sequence (SEQ ID NO : 1397) of a native sequence PR037730 cDN, 1397 is a clone designated herein as "DNA227267".

Figure 1398 shows the amino acid sequence (SEQ ID NO : 1398) derived from the coding sequence in Figure 1397.

Figure 1399 shows a nucleotide sequence (SEQ ID NO : 1399) of a native sequence PR038355 cDN 1399 is a clone designated herein as "DNA327920".

Figure 1400 shows the amino acid sequence (SEQ ID NO : 1400) derived from the coding sequence in Figure 1399.

Figure 1401 shows a nucleotide sequence (SEQ ID NO : 1401) of a native sequence PR083856 cDN 1401 is a clone designated herein as "DNA327921".

Figure 1402 shows the amino acid sequence (SEQ ID NO : 1402) derived from the coding sequence in Figure 1401.

Figure 1403 shows a nucleotide sequence (SEQ ID NO : 1403) of a native sequence PR083857 cDN 1403 is a clone designated herein as "DNA327922".

Figure 1404 shows the amino acid sequence (SEQ ID NO : 1404) derived from the coding sequence in Figure 1403.

Figure 1405 shows a nucleotide sequence (SEQ ID NO : 1405) of a native sequence PR06092 cDNA is a clone designated herein as "DNA327923".

Figure 1406 shows the amino acid sequence (SEQ ID NO : 1406) derived from the coding sequence in Figure 1405.

Figure 1407 shows a nucleotide sequence (SEQ ID NO : 1407) of a native sequence PR061855 cDN 1407 is a clone designated herein as "DNA273901".

Figure 1408 shows the amino acid sequence (SEQ ID NO : 1408) derived from the coding sequence in Figure 1407.

Figure 1409 shows a nucleotide sequence (SEQ ID NO : 1409) of a native sequence PRO12205 cDN 1409 is a clone designated herein as "DNA151848".

Figure 1410 shows the amino acid sequence (SEQ ID NO : 1410) derived from the coding sequence in Figure 1409.

Figure 1411 shows a nucleotide sequence (SEQ ID NO : 1411) of a native sequence PR058388 cDN 1411 is a clone designated herein as "DNA269992".

Figure 1412 shows the amino acid sequence (SEQ ID NO : 1412) derived from the coding sequence in Figure 1411..

Figure 1413 shows a nucleotide sequence (SEQ ID NO : 1413) of a native sequence PR083858 cDN 1413 is a clone designated herein as "DNA327924".

Figure 1414 shows the amino acid sequence (SEQ ID NO : 1414) derived from the coding sequence in Figure 1413.

Figure 1415 shows a nucleotide sequence (SEQ ID NO : 1415) of a native sequence PRO83859 cDN 1415 is a clone designated herein as "DNA327925".

Figure 1416 shows the amino acid sequence (SEQ ID NO : 1416) derived from the coding sequence in Figure 1415.

Figure 1417 shows a nucleotide sequence (SEQ ID NO : 1417) of a native sequence PRO83860 cDN 1417 is a clone designated herein as "DNA327926".

Figure 1418 shows the amino acid sequence (SEQ ID NO : 1418) derived from the coding sequence in Figure 1417.

Figure 1419 shows a nucleotide sequence (SEQ ID NO : 1419) of a native sequence PRO57311 cDN 1419 is a clone designated herein as "DNA327927".

Figure 1420 shows the amino acid sequence (SEQ ID NO : 1420) derived from the coding sequence in Figure 1419.

Figure 1421 shows a nucleotide sequence (SEQ ID NO : 1421) of a native sequence PRO1082 cDN 1421 is a clone designated herein as "DNA327928".

Figure 1422 shows the amino acid sequence (SEQ ID NO : 1422) derived from the coding sequence in Figure 1421.

Figure 1423 shows a nucleotide sequence (SEQ ID NO : 1423) of a native sequence cDNA, wherein designated herein as "DNA195869".

Figure 1424 shows a nucleotide sequence (SEQ ID NO : 1424) of a native sequence PRO83861 cDN 1424 is a clone designated herein as "DNA327929".

Figure 1425 shows the amino acid sequence (SEQ ID NO : 1425) derived from the coding sequence in Figure 1424.

Figure 1426 shows a nucleotide sequence (SEQ ID NO : 1426) of a native sequence PRO83862 cDN 1426 is a clone designated herein as "DNA327930".

Figure 1427 shows the amino acid sequence (SEQ ID NO : 1427) derived from the coding sequence in Figure 1426.

Figure 1428 shows a nucleotide sequence (SEQ ID NO : 1428) of a native sequence PRO83863 cDN 1428 is a clone designated herein as "DNA327931".

Figure 1429 shows the amino acid sequence (SEQ ID NO : 1429) derived from the coding sequence in Figure 1428.

Figure 1430 shows a nucleotide sequence (SEQ ID NO : 1430) of a native sequence cDNA, wherein designated herein as "DNA273119".

Figure 1431 shows a nucleotide sequence (SEQ ID NO : 1431) of a native sequence PR083864 cDN. 1431 is a clone designated herein as "DNA327932".

Figure 1432 shows the amino acid sequence (SEQ ID NO : 1432) derived from the coding sequence in Figure 1431.

Figure 1433 shows a nucleotide sequence (SEQ ID NO : 1433) of a native sequence PR062262 cDN. 1433 is a clone designated herein as "DNA274348".

Figure 1434 shows the amino acid sequence (SEQ ID NO : 1434) derived from the coding sequence in Figure 1433.

Figure 1435 shows a nucleotide sequence (SEQ ID NO : 1435) of a native sequence PR083865 cDN. 1435 is a clone designated herein as "DNA327933".

Figure 1436 shows the amino acid sequence (SEQ ID NO : 1436) derived from the coding sequence in Figure 1435.

Figure 1437 shows a nucleotide sequence (SEQ ID NO : 1437) of a native sequence PR04342 cDNA is a clone designated herein as "DNA327934".

Figure 1438 shows the amino acid sequence (SEQ ID NO : 1438) derived from the coding sequence in Figure 1437.

Figure 1439 shows a nucleotide sequence (SEQ ID NO : 1439) of a native sequence PRO1314 cDN. 1439 is a clone designated herein as "DNA324364".

Figure 1440 shows the amino acid sequence (SEQ ID NO : 1440) derived from the coding sequence in Figure 1439.

Figure 1441 shows a nucleotide sequence (SEQ ID NO : 1441) of a native sequence PR083866 cDN. 1441 is a clone designated herein as "DNA327935".

Figure 1442 shows the amino acid sequence (SEQ ID NO : 1442) derived from the coding sequence in Figure 1441.

Figure 1443 shows a nucleotide sequence (SEQ ID NO : 1443) of a native sequence PR0718 cDNA, is a clone designated herein as "DNA327936".

Figure 1444 shows the amino acid sequence (SEQ ID NO : 1444) derived from the coding sequence in Figure 1443.



Figure 1445 shows a nucleotide sequence (SEQ ID NO : 1445) of a native sequence PRO83867 cDNA 1445 is a clone designated herein as "DNA327937".

Figure 1446 shows the amino acid sequence (SEQ ID NO : 1446) derived from the coding sequence in Figure 1445.

Figure 1447 shows a nucleotide sequence (SEQ ID NO : 1447) of a native sequence PRO11577 cDNA 1447 is a clone designated herein as "DNA150654".

Figure 1448 shows the amino acid sequence (SEQ ID NO : 1448) derived from the coding sequence in Figure 1447.

Figure 1449 shows a nucleotide sequence (SEQ ID NO : 1449) of a native sequence PR083868 cDNA 1449 is a clone designated herein as "DNA327938".

Figure 1450 shows the amino acid sequence (SEQ ID NO : 1450) derived from the coding sequence in Figure 1449.

Figure 1451 shows a nucleotide sequence (SEQ ID NO : 1451) of a native sequence PRO83869 cDNA 1451 is a clone designated herein as "DNA327939".

Figure 1452 shows the amino acid sequence (SEQ ID NO : 1452) derived from the coding sequence in Figure 1451.

Figure 1453 shows a nucleotide sequence (SEQ ID NO : 1453) of a native sequence PR050262 cDNA 1453 is a clone designated herein as "DNA255183".

Figure 1454 shows the amino acid sequence (SEQ ID NO : 1454) derived from the coding sequence in Figure 1453.

Figure 1455 shows a nucleotide sequence (SEQ ID NO : 1455) of a native sequence PRO1375 cDNA 1455 is a clone designated herein as "DNA327940".

Figure 1456 shows the amino acid sequence (SEQ ID NO : 1456) derived from the coding sequence in Figure 1455.

Figure 1457 shows a nucleotide sequence (SEQ ID NO : 1457) of a native sequence PR0944 cDNA 1457 is a clone designated herein as "DNA327941".

Figure 1458 shows the amino acid sequence (SEQ ID NO : 1458) derived from the coding sequence in Figure 1457.

Figure 1459 shows a nucleotide sequence (SEQ ID NO : 1459) of a native sequence PR083870 cDNA 1459 is a clone designated herein as "DNA327942".

Figure 1460 shows the amino acid sequence (SEQ ID NO : 1460) derived from the coding sequence in Figure 1459.

Figure 1461 shows a nucleotide sequence (SEQ ID NO : 1461) of a native sequence PR0865 cDNA, is a clone designated herein as "DNA327943".

Figure 1462 shows the amino acid sequence (SEQ ID NO : 1462) derived from the coding sequence in Figure 1461.

Figure 1463 shows a nucleotide sequence (SEQ ID NO : 1463) of a native sequence PR07433 cDNA is a clone designated herein as "DNA327944".

Figure 1464 shows the amino acid sequence (SEQ ID NO : 1464) derived from the coding sequence in Figure.

Figure 1465 shows a nucleotide sequence (SEQ ID NO : 1465) of a native sequence PR082384 cDN 1465 is a clone designated herein as "DNA325936".

Figure 1466 shows the amino acid sequence (SEQ ID NO : 1466) derived from the coding sequence in Figure 1465.

Figure 1467 shows a nucleotide sequence (SEQ ID NO : 1467) of a native sequence PRO83871 cDN 1467 is a clone designated herein as "DNA327945".

Figure 1468 shows the amino acid sequence (SEQ ID NO : 1468) derived from the coding sequence in Figure 1467.

Figure 1469 shows a nucleotide sequence (SEQ ID NO : 1469) of a native sequence PR049401 cDN 1469 is a clone designated herein as "DNA254290".

Figure 1470 shows the amino acid sequence (SEQ ID NO : 1470) derived from the coding sequence in Figure 1469.

Figure 1471 shows a nucleotide sequence (SEQ ID NO : 1471) of a native sequence PRO83872 cDN 1471 is a clone designated herein as "DNA327946".

Figure 1472 shows the amino acid sequence (SEQ ID NO : 1472) derived from the coding sequence in Figure 1471.

Figure 1473 shows a nucleotide sequence (SEQ ID NO : 1473) of a native sequence PRO83873 cDN 1473 is a clone designated herein as "DNA327947".

Figure 1474 shows the amino acid sequence (SEQ ID NO : 1474) derived from the coding sequence in Figure 1473.

Figure 1475 shows a nucleotide sequence (SEQ ID NO : 1475) of a native sequence PRO10928 cDN 1475 is a clone designated herein as "DNA152786".

Figure 1476 shows the amino acid sequence (SEQ ID NO : 1476) derived from the coding sequence in Figure 1475.

Figure 1477 shows a nucleotide sequence (SEQ ID NO : 1477) of a native sequence PRO81339 cl 1477 is a clone designated herein as "DNA324707".

Figure 1478 shows the amino acid sequence (SEQ ID NO : 1478) derived from the coding sequence in Figure 1477.

Figure 1479 shows a nucleotide sequence (SEQ ID NO : 1479) of a native sequence PR069660 cl 1479 is a clone designated herein as "DNA327948".

Figure 1480 shows the amino acid sequence (SEQ ID NO : 1480) derived from the coding sequence in Figure 1479.

Figure 1481 shows a nucleotide sequence (SEQ ID NO : 1481) of a native sequence PRO83874 cl 1481 is a clone designated herein as "DNA327949".

Figure 1482 shows the amino acid sequence (SEQ ID NO : 1482) derived from the coding sequence in Figure 1481.

Figure 1483 shows a nucleotide sequence (SEQ ID NO : 1483) of a native sequence PR083875 cl 1483 is a clone designated herein as "DNA327950".

Figure 1484 shows the amino acid sequence (SEQ ID NO : 1484) derived from the coding sequence in Figure 1483.

Figure 1485 shows a nucleotide sequence (SEQ ID NO : 1485) of a native sequence PRO83876 cl 1485 is a clone designated herein as "DNA327951".

Figure 1486 shows the amino acid sequence (SEQ ID NO : 1486) derived from the coding sequence in Figure 1485.

Figure 1487 shows a nucleotide sequence (SEQ ID NO : 1487) of a native sequence PRO83877 cl 1487 is a clone designated herein as "DNA327952".

Figure 1488 shows the amino acid sequence (SEQ ID NO : 1488) derived from the coding sequence in Figure.

Figure 1489 shows a nucleotide sequence (SEQ ID NO : 1489) of a native sequence PRO83878 cl 1489 is a clone designated herein as "DNA327953".

Figure 1490 shows the amino acid sequence (SEQ ID NO : 1490) derived from the coding sequence in Figure 1489.

Figure 1491 shows a nucleotide sequence (SEQ ID NO : 1491) of a native sequence PR052040 cDN,  
1491 is a clone designated herein as "DNA257461".

Figure 1492 shows the amino acid sequence (SEQ ID NO : 1492) derived from the coding sequence  
in Figure 1491.

Figure 1493 shows a nucleotide sequence (SEQ ID NO : 1493) of a native sequence PRO83879 cDN  
1493 is a clone designated herein as "DNA327954".

Figure 1494 shows the amino acid sequence (SEQ ID NO : 1494) derived from the coding sequence  
in Figure 1493.

Figure 1495 shows a nucleotide sequence (SEQ ID NO : 1495) of a native sequence PRO83880 cDN  
1495 is a clone designated herein as "DNA327955".

Figure 1496 shows the amino acid sequence (SEQ ID NO : 1496) derived from the coding sequence  
in Figure 1495.

Figure 1497 shows a nucleotide sequence (SEQ ID NO : 1497) of a native sequence PRO83881 cDN  
1497 is a clone designated herein as "DNA327956".

Figure 1498 shows the amino acid sequence (SEQ ID NO : 1498) derived from the coding sequence  
in Figure 1497.

Figure 1499 shows a nucleotide sequence (SEQ ID NO : 1499) of a native sequence PRO83882 cDN,  
1499 is a clone designated herein as "DNA327957".

Figure 1500 shows the amino acid sequence (SEQ ID NO : 1500) derived from the coding sequence  
in Figure 1499.

Figure 1501 shows a nucleotide sequence (SEQ ID NO : 1501) of a native sequence PRO82861 cDN,  
1501 is a clone designated herein as "DNA326483".

Figure 1502 shows the amino acid sequence (SEQ ID NO : 1502) derived from the coding sequence c  
in Figure 1501.

Figure 1503 shows a nucleotide sequence (SEQ ID NO : 1503) of a native sequence PRO50738 cDN,  
1503 is a clone designated herein as "DNA255676".

Figure 1504 shows the amino acid sequence (SEQ ID NO : 1504) derived from the coding sequence  
in Figure 1503.

Figure 1505 shows a nucleotide sequence (SEQ ID NO : 1505) of a native sequence PR061417 cDN/  
1505 is a clone designated herein as "DNA273418".

Figure 1506 shows the amino acid sequence (SEQ ID NO : 1506) derived from the coding sequence  
in Figure 1505

Figure 1507 shows a nucleotide sequence (SEQ ID NO : 1507) of a native sequence PRO23554 cDN,  
1507 is a clone designated herein as "DNA327958".

Figure 1508 shows the amino acid sequence (SEQ ID NO : 1508) derived from the coding sequence ,  
in Figure 1507.

Figure 1509 shows a nucleotide sequence (SEQ ID NO : 1509) of a native sequence PRO83883 cDN,  
1509 is a clone designated herein as "DNA327959".

Figure 1510 shows the amino acid sequence (SEQ ID NO : 1510) derived from the coding sequence ,  
in Figure 1509.

Figure 1511 shows a nucleotide sequence (SEQ ID NO : 1511) of a native sequence PRO52449 cDN,  
1511 is a clone designated herein as "DNA257916".

Figure 1512 shows the amino acid sequence (SEQ ID NO : 1512) derived from the coding sequence ,  
in Figure 1511.

Figure 1513 shows a nucleotide sequence (SEQ ID NO : 1513) of a native sequence PRO83884 cDN  
1513 is a clone designated herein as "DNA327960".

Figure 1514 shows the amino acid sequence (SEQ ID NO : 1514) derived from the coding sequence ,  
in Figure.

Figure 1515 shows a nucleotide sequence (SEQ ID NO : 1515) of a native sequence PRO83885 cDN  
1515 is a clone designated herein as "DNA327961".

Figure 1516 shows the amino acid sequence (SEQ ID NO : 1516) derived from the coding sequence ,  
in Figure 1515.

Figure 1517 shows a nucleotide sequence (SEQ ID NO : 1517) of a native sequence PRO54660 cDN  
1517 is a clone designated herein as "DNA327962".

Figure 1518 shows the amino acid sequence (SEQ ID NO : 1518) derived from the coding sequence ,  
in Figure 1517.

Figure 1519 shows a nucleotide sequence (SEQ ID NO : 1519) of a native sequence PRO83886 cDN  
1519 is a clone designated herein as "DNA327963".

Figure 1520 shows the amino acid sequence (SEQ ID NO : 1520) derived from the coding sequence ,  
in Figure 1519.

Figure 1521 shows a nucleotide sequence (SEQ ID NO : 1521) of a native sequence PRO83887 cDN  
1521 is a clone designated herein as "DNA327964".

Figure 1522 shows the amino acid sequence (SEQ ID NO : 1522) derived from the coding sequence in Figure 1521.

Figure 1523 shows a nucleotide sequence (SEQ ID NO : 1523) of a native sequence PRO83888. 1523 is a clone designated herein as "DNA327965".

Figure 1524 shows the amino acid sequence (SEQ ID NO : 1524) derived from the coding sequence in Figure 1523.

Figure 1525 shows a nucleotide sequence (SEQ ID NO : 1525) of a native sequence PR083889. 1525 is a clone designated herein as "DNA327966".

Figure 1526 shows the amino acid sequence (SEQ ID NO : 1526) derived from the coding sequence in Figure 1525.

Figure 1527 shows a nucleotide sequence (SEQ ID NO : 1527) of a native sequence PRO1065. 1527 is a clone designated herein as "DNA327200".

Figure 1528 shows the amino acid sequence (SEQ ID NO : 1528) derived from the coding sequence in Figure 1527.

Figure 1529 shows a nucleotide sequence (SEQ ID NO : 1529) of a native sequence PRO83890. 1529 is a clone designated herein as "DNA327967".

Figure 1530 shows the amino acid sequence (SEQ ID NO : 1530) derived from the coding sequence in Figure 1529.

Figure 1531 shows a nucleotide sequence (SEQ ID NO : 1531) of a native sequence PRO83891. 1531 is a clone designated herein as "DNA327968".

Figure 1532 shows the amino acid sequence (SEQ ID NO : 1532) derived from the coding sequence in Figure 1531.

Figure 1533 shows a nucleotide sequence (SEQ ID NO : 1533) of a native sequence PR0301. 1533 is a clone designated herein as "DNA327969".

Figure 1534 shows the amino acid sequence (SEQ ID NO : 1534) derived from the coding sequence in Figure 1533.

Figure 1535 shows a nucleotide sequence (SEQ ID NO : 1535) of a native sequence PR083473. 1535 is a clone designated herein as "DNA327197".

Figure 1536 shows the amino acid sequence (SEQ ID NO : 1536) derived from the coding sequence in Figure 1535.

Figure 1537 shows a nucleotide sequence (SEQ ID NO : 1537) of a native sequence PR083892. 1537 is a clone designated herein as "DNA327970".

Figure 1538 shows the amino acid sequence (SEQ ID NO : 1538) derived from the coding sequence in Figure 1537.

Figure 1539 shows a nucleotide sequence (SEQ ID NO : 1539) of a native sequence PR083893 cDN 1539 is a clone designated herein as "DNA327971".

Figure 1540 shows the amino acid sequence (SEQ ID NO : 1540) derived from the coding sequence in Figure 1539.

Figure 1541 shows a nucleotide sequence (SEQ ID NO : 1541) of a native sequence PR083474 cDN 1541 is a clone designated herein as "DNA327198".

Figure 1542 shows the amino acid sequence (SEQ ID NO : 1542) derived from the coding sequence in Figure 1541.

Figure 1543 shows a nucleotide sequence (SEQ ID NO : 1543) of a native sequence PR083894 cDN 1543 is a clone designated herein as "DNA327972".

Figure 1544 shows the amino acid sequence (SEQ ID NO : 1544) derived from the coding sequence in Figure 1543.

Figure 1545 shows a nucleotide sequence (SEQ ID NO : 1545) of a native sequence PR083895 cDN 1545 is a clone designated herein as "DNA327973".

Figure 1546 shows the amino acid sequence (SEQ ID NO : 1546) derived from the coding sequence in Figure 1545.

Figure 1547 shows a nucleotide sequence (SEQ ID NO : 1547) of a native sequence PR083896 cDN 1547 is a clone designated herein as "DNA327974".

Figure 1548 shows the amino acid sequence (SEQ ID NO : 1548) derived from the coding sequence in Figure 1547.

Figure 1549 shows a nucleotide sequence (SEQ ID NO : 1549) of a native sequence PR083897 cDN 1549 is a clone designated herein as "DNA327975".

Figure 1550 shows the amino acid sequence (SEQ ID NO : 1550) derived from the coding sequence in Figure 1549.

Figure 1551 shows a nucleotide sequence (SEQ ID NO : 1551) of a native sequence PR069574 cDN 1551 is a clone designated herein as "DNA327976".

Figure 1552 shows the amino acid sequence (SEQ ID NO : 1552) derived from the coding sequence in Figure 1521.

Figure 1553 shows a nucleotide sequence (SEQ ID NO : 1553) of a native sequence PRO83898  
1553 is a clone designated herein as "DNA327977".

Figure 1554 shows the amino acid sequence (SEQ ID NO : 1554) derived from the coding sequence  
in Figure 1553.

Figure 1555 shows a nucleotide sequence (SEQ ID NO : 1555) of a native sequence PRO83899  
1555 is a clone designated herein as "DNA327978".

Figure 1556 shows the amino acid sequence (SEQ ID NO : 1556) derived from the coding sequence  
in Figure 1555.

Figure 1557 shows a nucleotide sequence (SEQ ID NO : 1557) of a native sequence PRO82633  
1557 is a clone designated herein as "DNA327979".

Figure 1558 shows the amino acid sequence (SEQ ID NO : 1558) derived from the coding sequence  
in Figure 1557.

Figure 1559 shows a nucleotide sequence (SEQ ID NO : 1559) of a native sequence PRO83900  
1559 is a clone designated herein as "DNA327980".

Figure 1560 shows the amino acid sequence (SEQ ID NO : 1560) derived from the coding sequence  
in Figure 1559.

Figure 1561 shows a nucleotide sequence (SEQ ID NO : 1561) of a native sequence PRO83901  
1561 is a clone designated herein as "DNA327981".

Figure 1562 shows the amino acid sequence (SEQ ID NO : 1562) derived from the coding sequence  
in Figure 1561.

Figure 1563 shows a nucleotide sequence (SEQ ID NO : 1563) of a native sequence PRO83902  
1563 is a clone designated herein as "DNA327982".

Figure 1564 shows the amino acid sequence (SEQ ID NO : 1654) derived from the coding sequence  
in Figure 1563.

Figure 1565 shows a nucleotide sequence (SEQ ID NO : 1565) of a native sequence PRO83903  
1565 is a clone designated herein as "DNA327983".

Figure 1566 shows the amino acid sequence (SEQ ID NO : 1566) derived from the coding sequence  
in Figure 1565.

Figure 1567 shows a nucleotide sequence (SEQ ID NO : 1567) of a native sequence PRO83904  
1567 is a clone designated herein as "DNA327984".

Figure 1568 shows the amino acid sequence (SEQ ID NO : 1568) derived from the coding sequence  
in Figure 1567.



Figure 1569 shows a nucleotide sequence (SEQ ID NO : 1569) of a native sequence PR023253 cDN, 1569 is a clone designated herein as "DNA169523".

Figure 1570 shows the amino acid sequence (SEQ ID NO : 1570) derived from the coding sequence , in Figure 1569.

Figure 1571 shows a nucleotide sequence (SEQ ID NO : 1571) of a native sequence PR083905 cDN 1571 is a clone designated herein as "DNA327985".

Figure 1572 shows the amino acid sequence (SEQ ID NO : 1572) derived from the coding sequence , in Figure 1571.

Figure 1573 shows a nucleotide sequence (SEQ ID NO : 1573) of a native sequence PR083906 cDN, 1573 is a clone designated herein as "DNA327986".

Figure 1574 shows the amino acid sequence (SEQ ID NO : 1574) derived from the coding sequence , in Figure 1573.

Figure 1575 shows a nucleotide sequence (SEQ ID NO : 1575) of a native sequence PR083907 cDN, 1575 is a clone designated herein as "DNA327987".

Figure 1576 shows the amino acid sequence (SEQ ID NO : 1576) derived from the coding sequence , in Figure 1575.

Figure 1577 shows a nucleotide sequence (SEQ ID NO : 1577) of a native sequence PR083908 cDN, 1577 is a clone designated herein as "DNA327988".

Figure 1578 shows the amino acid sequence (SEQ ID NO : 1578) derived from the coding sequence , in Figure 1577.

Figure 1579 shows a nucleotide sequence (SEQ ID NO : 1579) of a native sequence PR083909 cDN 1579 is a clone designated herein as "DNA327989".

Figure 1580 shows the amino acid sequence (SEQ ID NO : 1580) derived from the coding sequence , in Figure 1579.

Figure 1581 shows a nucleotide sequence (SEQ ID NO : 1581) of a native sequence PR083910 cDN, 1581 is a clone designated herein as "DNA327990".

Figure 1582 shows the amino acid sequence (SEQ ID NO : 1582) derived from the coding sequence , in Figure 1581.

Figure 1583 shows a nucleotide sequence (SEQ ID NO : 1583) of a native sequence cDNA, wherein : designated herein as "DNA327991".

Figure 1584 shows a nucleotide sequence (SEQ ID NO : 1584) of a native sequence PRO83912 1584 is a clone designated herein as "DNA327992".

Figure 1585 shows the amino acid sequence (SEQ ID NO : 1585) derived from the coding sequence in Figure 1584.

Figure 1586 shows a nucleotide sequence (SEQ ID NO : 1586) of a native sequence PRO81138, 1586 is a clone designated herein as "DNA327993".

Figure 1587 shows the amino acid sequence (SEQ ID NO : 1587) derived from the coding sequence in Figure 1586.

Figure 1588 shows a nucleotide sequence (SEQ ID NO : 1588) of a native sequence cDNA, which is designated herein as "DNA327994".

Figure 1589 shows a nucleotide sequence (SEQ ID NO : 1589) of a native sequence PRO83914, 1589 is a clone designated herein as "DNA327995".

Figure 1590 shows the amino acid sequence (SEQ ID NO : 1590) derived from the coding sequence in Figure 1589.

Figure 1591 shows a nucleotide sequence (SEQ ID NO : 1591) of a native sequence PRO83915, 1591 is a clone designated herein as "DNA327996".

Figure 1592 shows the amino acid sequence (SEQ ID NO : 1592) derived from the coding sequence in Figure 1591.

Figure 1593 shows a nucleotide sequence (SEQ ID NO : 1593) of a native sequence PRO83916 1593 is a clone designated herein as "DNA327997".

Figure 1594 shows the amino acid sequence (SEQ ID NO : 1594) derived from the coding sequence in Figure 1593.

Figure 1595 shows a nucleotide sequence (SEQ ID NO : 1595) of a native sequence cDNA, which is designated herein as "DNA327998".

Figure 1596 shows a nucleotide sequence (SEQ ID NO : 1596) of a native sequence PRO83918 1596 is a clone designated herein as "DNA327999".

Figure 1597 shows the amino acid sequence (SEQ ID NO : 1597) derived from the coding sequence in Figure 1596.

Figure 1598 shows a nucleotide sequence (SEQ ID NO : 1598) of a native sequence PRO83919, 1598 is a clone designated herein as "DNA328000".

Figure 1599 shows the amino acid sequence (SEQ ID NO : 1599) derived from the coding sequence in Figure 1598.

Figure 1600 shows a nucleotide sequence (SEQ ID NO : 1600) of a native sequence PRO83920 c1600 is a clone designated herein as "DNA328001".

Figure 1601 shows the amino acid sequence (SEQ ID NO : 1601) derived from the coding sequence in Figure 1600.

Figure 1602 shows a nucleotide sequence (SEQ ID NO : 1602) of a native sequence PRO83921 c1602 is a clone designated herein as "DNA328002".

Figure 1603 shows the amino acid sequence (SEQ ID NO : 1603) derived from the coding sequence in Figure 1602.

Figure 1604 shows a nucleotide sequence (SEQ ID NO : 1604) of a native sequence PRO83922 c1604 is a clone designated herein as "DNA328003".

Figure 1605 shows the amino acid sequence (SEQ ID NO : 1605) derived from the coding sequence in Figure 1604.

Figure 1606 shows a nucleotide sequence (SEQ ID NO : 1606) of a native sequence PRO83923 c1606 is a clone designated herein as "DNA328004".

Figure 1607 shows the amino acid sequence (SEQ ID NO : 1607) derived from the coding sequence in Figure 1606.

Figure 1608 shows a nucleotide sequence (SEQ ID NO : 1608) of a native sequence cDNA, where designated herein as "DNA328005".

Figure 1609 shows a nucleotide sequence (SEQ ID NO : 1509) of a native sequence PRO83924 c1609 is a clone designated herein as "DNA328006".

Figure 1610 shows the amino acid sequence (SEQ ID NO : 1610) derived from the coding sequence in Figure 1609.

Figure 1611 shows a nucleotide sequence (SEQ ID NO : 1611) of a native sequence cDNA, where designated herein as "DNA255056".

Figure 1612 shows a nucleotide sequence (SEQ ID NO : 1612) of a native sequence PRO83925 c1612 is a clone designated herein as "DNA328007".

Figure 1613 shows the amino acid sequence (SEQ ID NO : 1613) derived from the coding sequence in Figure 1612.

Figure 1614 shows a nucleotide sequence (SEQ ID NO : 1614) of a native sequence PRO83926 c1614 is a clone designated herein as "DNA328008".

Figure 1615 shows the amino acid sequence (SEQ ID NO : 1615) derived from the coding sequence in Figure 1614.

Figure 1616 shows a nucleotide sequence (SEQ ID NO : 1616) of a native sequence PR083927 cDN 1616 is a clone designated herein as "DNA328009".

Figure 1617 shows the amino acid sequence (SEQ ID NO : 1617) derived from the coding sequence in Figure 1616.

Figure 1618 shows a nucleotide sequence (SEQ ID NO : 1618) of a native sequence PR083928 cDN 1618 is a clone designated herein as "DNA328010".

Figure 1619 shows the amino acid sequence (SEQ ID NO : 1619) derived from the coding sequence in Figure 1618.

Figure 1620 shows a nucleotide sequence (SEQ ID NO : 1620) of a native sequence PR028545 cDN 1620 is a clone designated herein as "DNA199088".

Figure 1621 shows the amino acid sequence (SEQ ID NO : 1621) derived from the coding sequence in Figure 1620.

Figure 1622 shows a nucleotide sequence (SEQ ID NO : 1622) of a native sequence PR070021 cDN 1622 is a clone designated herein as "DNA288261".

Figure 1623 shows the amino acid sequence (SEQ ID NO : 1623) derived from the coding sequence in Figure 1622.

Figure 1624 shows a nucleotide sequence (SEQ ID NO : 1624) of a native sequence PR083929 cDN 1624 is a clone designated herein as "DNA328011".

Figure 1625 shows the amino acid sequence (SEQ ID NO : 1625) derived from the coding sequence in Figure 1624.

Figure 1626 shows a nucleotide sequence (SEQ ID NO : 1626) of a native sequence PR083930 cDN 1626 is a clone designated herein as "DNA328012".

Figure 1627 shows the amino acid sequence (SEQ ID NO : 1627) derived from the coding sequence in Figure 1626.

Figure 1628 shows a nucleotide sequence (SEQ ID NO : 1628) of a native sequence PR083931 cDN 1628 is a clone designated herein as "DNA328013".

Figure 1629 shows the amino acid sequence (SEQ ID NO : 1629) derived from the coding sequence in Figure 1628.

Figure 1630 shows a nucleotide sequence (SEQ ID NO : 1630) of a native sequence PR083932 cDN 1630 is a clone designated herein as "DNA328014".

Figure 1631 shows the amino acid sequence (SEQ ID NO : 1631) derived from the coding sequence in Figure 1630.

Figure 1632 shows a nucleotide sequence (SEQ ID NO : 1632) of a native sequence PR050889 cDN 1632 is a clone designated herein as "DNA255834".

Figure 1633 shows the amino acid sequence (SEQ ID NO : 1633) derived from the coding sequence in Figure 1632.

Figure 1634 shows a nucleotide sequence (SEQ ID NO : 1634) of a native sequence PR0865 cDNA, is a clone designated herein as "DNA260947".

Figure 1635 shows the amino acid sequence (SEQ ID NO : 1635) derived from the coding sequence in Figure 1634.

Figure 1636 shows a nucleotide sequence (SEQ ID NO : 1636) of a native sequence PRO83933 cDN 1636 is a clone designated herein as "DNA328015".

Figure 1637 shows the amino acid sequence (SEQ ID NO : 1637) derived from the coding sequence in Figure 1636.

Figure 1638 shows a nucleotide sequence (SEQ ID NO : 1638) of a native sequence PR083934 cDN 1638 is a clone designated herein as "DNA328016".

Figure 1639 shows the amino acid sequence (SEQ ID NO : 1639) derived from the coding sequence in Figure 1638.

Figure 1640 shows a nucleotide sequence (SEQ ID NO : 1640) of a native sequence PRO83935 cDN 1640 is a clone designated herein as "DNA328017".

Figure 1641 shows the amino acid sequence (SEQ ID NO : 1641) derived from the coding sequence in Figure 1640.

Figure 1642 shows a nucleotide sequence (SEQ ID NO : 1642) of a native sequence PRO83936 cDN 1642 is a clone designated herein as "DNA328018".

Figure 1643 shows the amino acid sequence (SEQ ID NO : 1643) derived from the coding sequence in Figure 1642.

Figure 1644 shows a nucleotide sequence (SEQ ID NO : 1644) of a native sequence PR083937 cDN 1644 is a clone designated herein as "DNA328019".

Figure 1645 shows the amino acid sequence (SEQ ID NO : 1645) derived from the coding sequence in Figure 1643.

Figure 1646 shows a nucleotide sequence (SEQ ID NO : 1646) of a native sequence PRO83938 1646 is a clone designated herein as "DNA328020".

Figure 1647 shows the amino acid sequence (SEQ ID NO : 1647) derived from the coding sequence in Figure 1646.

Figure 1648 shows a nucleotide sequence (SEQ ID NO : 1648) of a native sequence cDNA, which is designated herein as "DNA268880".

Figure 1649 shows a nucleotide sequence (SEQ ID NO : 1649) of a native sequence PRO1190 c 1649 is a clone designated herein as "DNA59586".

Figure 1650 shows the amino acid sequence (SEQ ID NO : 1650) derived from the coding sequence in Figure 1649.

Figure 1651 shows a nucleotide sequence (SEQ ID NO : 1651) of a native sequence cDNA, which is designated herein as "DNA328021".

Figure 1652 shows a nucleotide sequence (SEQ ID NO : 1652) of a native sequence cDNA, which is designated herein as "DNA328022".

Figure 1653 shows a nucleotide sequence (SEQ ID NO : 1653) of a native sequence PRO61223 1653 is a clone designated herein as "DNA328023".

Figure 1654 shows the amino acid sequence (SEQ ID NO : 1654) derived from the coding sequence in Figure 1653.

Figure 1655 shows a nucleotide sequence (SEQ ID NO : 1655) of a native sequence PRO83941 1655 is a clone designated herein as "DNA328024".

Figure 1656 shows the amino acid sequence (SEQ ID NO : 1656) derived from the coding sequence in Figure 1655.

Figure 1657 shows a nucleotide sequence (SEQ ID NO : 1657) of a native sequence PRO83942 1657 is a clone designated herein as "DNA328025".

Figure 1658 shows the amino acid sequence (SEQ ID NO : 1658) derived from the coding sequence in Figure 1657.

Figure 1659 shows a nucleotide sequence (SEQ ID NO : 1659) of a native sequence PRO83943 1659 is a clone designated herein as "DNA328026".

Figure 1660 shows the amino acid sequence (SEQ ID NO : 1660) derived from the coding sequence in Figure 1659.

Figure 1661 shows a nucleotide sequence (SEQ ID NO : 1661) of a native sequence PRO23314 1661 is a clone designated herein as "DNA103806".

Figure 1662 shows the amino acid sequence (SEQ ID NO : 1662) derived from the coding sequence in Figure 1661.

Figure 1663 shows a nucleotide sequence (SEQ ID NO : 1663) of a native sequence PRO83944 cDN-1663 is a clone designated herein as "DNA328027".

Figure 1664 shows the amino acid sequence (SEQ ID NO : 1664) derived from the coding sequence in Figure 1663.

Figure 1665 shows a nucleotide sequence (SEQ ID NO : 1665) of a native sequence PRO83945 cDN-1665 is a clone designated herein as "DNA328028".

Figure 1666 shows the amino acid sequence (SEQ ID NO : 1666) derived from the coding sequence in Figure 1665.

Figure 1667 shows a nucleotide sequence (SEQ ID NO : 1667) of a native sequence PRO83946 cDN-1667 is a clone designated herein as "DNA328029".

Figure 1668 shows the amino acid sequence (SEQ ID NO : 1668) derived from the coding sequence in Figure 1667.

Figure 1669 shows a nucleotide sequence (SEQ ID NO : 1669) of a native sequence PR04977 cDNA is a clone designated herein as "DNA62849".

Figure 1670 shows the amino acid sequence (SEQ ID NO : 1670) derived from the coding sequence in Figure 1669.

Figure 1671 shows a nucleotide sequence (SEQ ID NO : 1671) of a native sequence PRO83947 cDN-1671 is a clone designated herein as "DNA328030".

Figure 1672 shows the amino acid sequence (SEQ ID NO : 1672) derived from the coding sequence in Figure 1671.

Figure 1673 shows a nucleotide sequence (SEQ ID NO : 1673) of a native sequence PRO83948 cDN-1673 is a clone designated herein as "DNA328031".

Figure 1674 shows the amino acid sequence (SEQ ID NO : 1674) derived from the coding sequence in Figure 1673.

Figure 1675 shows a nucleotide sequence (SEQ ID NO : 1675) of a native sequence PR071114 cDN-1675 is a clone designated herein as "DNA328032".

Figure 1676 shows the amino acid sequence (SEQ ID NO : 1676) derived from the coding sequence in Figure 1675.

Figure 1677 shows a nucleotide sequence (SEQ ID NO : 1677) of a native sequence PR083949 cDN, 1677 is a clone designated herein as "DNA328033".

Figure 1678 shows the amino acid sequence (SEQ ID NO : 1678) derived from the coding sequence , in Figure 1677.

Figure 1679 shows a nucleotide sequence (SEQ ID NO : 1679) of a native sequence PR083950 cDN, 1679 is a clone designated herein as "DNA328034".

Figure 1680 shows the amino acid sequence (SEQ ID NO : 1680) derived from the coding sequence , in Figure 1679.

Figure 1681 shows a nucleotide sequence (SEQ ID NO : 1681) of a native sequence PR083951 cDN, 1681 is a clone designated herein as "DNA328035".

Figure 1682 shows the amino acid sequence (SEQ ID NO : 1682) derived from the coding sequence , in Figure 1681.

Figure 1683 shows a nucleotide sequence (SEQ ID NO : 1683) of a native sequence cDNA, wherein : designated herein as "DNA328036".

Figure 1684 shows a nucleotide sequence (SEQ ID NO : 1684) of a native sequence cDNA, wherein : designated herein as "DNA328037".

Figure 1685 shows a nucleotide sequence (SEQ ID NO : 1685) of a native sequence PRO83953 cDN 1685 is a clone designated herein as "DNA328038".

Figure 1686 shows the amino acid sequence (SEQ ID NO : 1686) derived from the coding sequence , in Figure 1685.

Figure 1687 shows a nucleotide sequence (SEQ ID NO : 1687) of a native sequence PR083954 cDN, 1687 is a clone designated herein as "DNA328039".

Figure 1688 shows the amino acid sequence (SEQ ID NO : 1688) derived from the coding sequence , in Figure 1677.

Figure 1689 shows a nucleotide sequence (SEQ ID NO : 1689) of a native sequence cDNA, wherein : designated herein as "DNA328040".

Figure 1690 shows a nucleotide sequence (SEQ ID NO : 1690) of a native sequence PR083955 cDN, 1690 is a clone designated herein as "DNA328041".

Figure 1691 shows the amino acid sequence (SEQ ID NO : 1691) derived from the coding sequence , in Figure 1690.

Figure 1692 shows a nucleotide sequence (SEQ ID NO : 1692) of a native sequence PR083956 cDN, 1692 is a clone designated herein as "DNA328042".



Figure 1693 shows the amino acid sequence (SEQ ID NO : 1693) derived from the coding sequence in Figure 1692.

Figure 1694 shows a nucleotide sequence (SEQ ID NO : 1694) of a native sequence PR083957 cDN 1694 is a clone designated herein as "DNA328043".

Figure 1695 shows the amino acid sequence (SEQ ID NO : 1695) derived from the coding sequence in Figure 1694.

Figure 1696 shows a nucleotide sequence (SEQ ID NO : 1696) of a native sequence PR083958 cDN 1696 is a clone designated herein as "DNA328044".

Figure 1697 shows the amino acid sequence (SEQ ID NO:1697) derived from the coding sequence o in Figure 1696.

Figure 1698 shows a nucleotide sequence (SEQ ID NO : 1698) of a native sequence PR083959 cDN 1698 is a clone designated herein as "DNA328045".

Figure 1699 shows the amino acid sequence (SEQ ID NO : 1699) derived from the coding sequence in Figure 1698.

Figure 1700 shows a nucleotide sequence (SEQ ID NO : 1700) of a native sequence PRO83960 cDN 1700 is a clone designated herein as "DNA328046".

Figure 1701 shows the amino acid sequence (SEQ ID NO : 1701) derived from the coding sequence in Figure 1700.

Figure 1702 shows a nucleotide sequence (SEQ ID NO : 1702) of a native sequence PR083961 cDN 1702 is a clone designated herein as "DNA328047".

Figure 1703 shows the amino acid sequence (SEQ ID NO : 1703) derived from the coding sequence in Figure 1702.

Figure 1704 shows a nucleotide sequence (SEQ ID NO : 1704) of a native sequence PR083962 cDN 1704 is a clone designated herein as "DNA328048".

Figure 1705 shows the amino acid sequence (SEQ ID NO : 1705) derived from the coding sequence in Figure 1704.

Figure 1706 shows a nucleotide sequence (SEQ ID NO : 1706) of a native sequence cDNA, wherein designated herein as "DNA257403".

Figure 1707 shows a nucleotide sequence (SEQ ID NO : 1707) of a native sequence PR023317 cDN 1707 is a clone designated herein as "DNA193899".

Figure 1708 shows the amino acid sequence (SEQ ID NO : 1708) derived from the coding sequence in Figure 1707.

Figure 1709 shows a nucleotide sequence (SEQ ID NO : 1709) of a native sequence PRO83963 1709 is a clone designated herein as "DNA328049".

Figure 1710 shows the amino acid sequence (SEQ ID NO : 1710) derived from the coding sequence in Figure 1709.

Figure 1711 shows a nucleotide sequence (SEQ ID NO : 1711) of a native sequence PRO60890, 1711 is a clone designated herein as "DNA272784".

Figure 1712 shows the amino acid sequence (SEQ ID NO : 1712) derived from the coding sequence in Figure 1711.

Figure 1713 shows a nucleotide sequence (SEQ ID NO : 1713) of a native sequence PRO49544, 1713 is a clone designated herein as "DNA254435".

Figure 1714 shows the amino acid sequence (SEQ ID NO : 1714) derived from the coding sequence in Figure 1713.

Figure 1715 shows a nucleotide sequence (SEQ ID NO : 1715) of a native sequence PRO83964 1715 is a clone designated herein as "DNA328050".

Figure 1716 shows the amino acid sequence (SEQ ID NO : 1716) derived from the coding sequence in Figure 1715.

Figure 1717 shows a nucleotide sequence (SEQ ID NO : 1717) of a native sequence PRO83965 1717 is a clone designated herein as "DNA328051".

Figure 1718 shows the amino acid sequence (SEQ ID NO : 1718) derived from the coding sequence in Figure 1717.

Figure 1719 shows a nucleotide sequence (SEQ ID NO : 1719) of a native sequence PRO83966 1719 is a clone designated herein as "DNA328052".

Figure 1720 shows the amino acid sequence (SEQ ID NO : 1720) derived from the coding sequence in Figure 1719.

Figure 1721 shows a nucleotide sequence (SEQ ID NO : 1721) of a native sequence PRO61074, 1721 is a clone designated herein as "DNA273002".

Figure 1722 shows the amino acid sequence (SEQ ID NO : 1722) derived from the coding sequence in Figure 1721.

Figure 1723 shows a nucleotide sequence (SEQ ID NO : 1723) of a native sequence cDNA, designated herein as "DNA164635".

Figure 1724 shows a nucleotide sequence (SEQ ID NO : 1724) of a native sequence PRO83967 c1 1724 is a clone designated herein as "DNA328053".

Figure 1725 shows the amino acid sequence (SEQ ID NO : 1725) derived from the coding sequence in Figure 1724.

Figure 1726 shows a nucleotide sequence (SEQ ID NO : 1726) of a native sequence PRO19908 c1 1726 is a clone designated herein as "DNA76526".

Figure 1727 shows the amino acid sequence (SEQ ID NO : 1727) derived from the coding sequence in Figure 1726.

Figure 1728 shows a nucleotide sequence (SEQ ID NO : 1728) of a native sequence PRO11861 c1 1728 is a clone designated herein as "DNA151516".

Figure 1729 shows the amino acid sequence (SEQ ID NO : 1729) derived from the coding sequence in Figure 1728.

Figure 1730 shows a nucleotide sequence (SEQ ID NO : 1730) of a native sequence PR083968 c1 1730 is a clone designated herein as "DNA328054".

Figure 1731 shows the amino acid sequence (SEQ ID NO : 1731) derived from the coding sequence in Figure 1730.

Figure 1732 shows a nucleotide sequence (SEQ ID NO : 1732) of a native sequence PRO83969 c1 1732 is a clone designated herein as "DNA328055".

Figure 1733 shows the amino acid sequence (SEQ ID NO : 1733) derived from the coding sequence in Figure 1732.

Figure 1734 shows a nucleotide sequence (SEQ ID NO : 1734) of a native sequence PRO83970 c1 1734 is a clone designated herein as "DNA328056".

Figure 1735 shows the amino acid sequence (SEQ ID NO : 1735) derived from the coding sequence in Figure 1734.

Figure 1736 shows a nucleotide sequence (SEQ ID NO : 1736) of a native sequence cDNA, where designated herein as "DNA328057".

Figure 1737 shows a nucleotide sequence (SEQ ID NO : 1737) of a native sequence PRO83971 c1 1737 is a clone designated herein as "DNA328058".

Figure 1738 shows the amino acid sequence (SEQ ID NO : 1738) derived from the coding sequence in Figure 1737.

Figure 1739 shows a nucleotide sequence (SEQ ID NO : 1739) of a native sequence PR052268 cDN, 1739 is a clone designated herein as "DNA257714".

Figure 1740 shows the amino acid sequence (SEQ ID NO : 1740) derived from the coding sequence, in Figure 1739.

Figure 1741 shows a nucleotide sequence (SEQ ID NO : 1741) of a native sequence PR083972 cDN, 1741 is a clone designated herein as "DNA328059".

Figure 1742 shows the amino acid sequence (SEQ ID NO : 1742) derived from the coding sequence, in Figure 1741.

Figure 1743 shows a nucleotide sequence (SEQ ID NO : 1743) of a native sequence PR083973 cDN, 1743 is a clone designated herein as "DNA328060".

Figure 1744 shows the amino acid sequence (SEQ ID NO : 1744) derived from the coding sequence, in Figure 1743.

Figure 1745 shows a nucleotide sequence (SEQ ID NO : 1745) of a native sequence PR083974 cDN, 1745 is a clone designated herein as "DNA328061".

Figure 1746 shows the amino acid sequence (SEQ ID NO : 1746) derived from the coding sequence, in Figure 1745.

Figure 1747 shows a nucleotide sequence (SEQ ID NO : 1747) of a native sequence PR083975 cDN, 1747 is a clone designated herein as "DNA328062".

Figure 1748 shows the amino acid sequence (SEQ ID NO : 1748) derived from the coding sequence, in Figure 1747.

Figure 1749 shows a nucleotide sequence (SEQ ID NO : 1749) of a native sequence PR083976 cDN, 1749 is a clone designated herein as "DNA328063".

Figure 1750 shows the amino acid sequence (SEQ ID NO : 1750) derived from the coding sequence, in Figure 1749.

Figure 1751 shows a nucleotide sequence (SEQ ID NO : 1751) of a native sequence PR03446 cDNA is a clone designated herein as "DNA92219".

Figure 1752 shows the amino acid sequence (SEQ ID NO : 1752) derived from the coding sequence, in Figure 1751.

Figure 1753 shows a nucleotide sequence (SEQ ID NO : 1753) of a native sequence PR083977 cDN, 1753 is a clone designated herein as "DNA328064".

Figure 1754 shows the amino acid sequence (SEQ ID NO : 1754) derived from the coding sequence c in Figure 1753

Figure 1755 shows a nucleotide sequence (SEQ ID NO : 1755) of a native sequence PR083978 cDN, 1755 is a clone designated herein as "DNA328065".

Figure 1756 shows the amino acid sequence (SEQ ID NO : 1756) derived from the coding sequence ( in Figure 1755.

Figure 1757 shows a nucleotide sequence (SEQ ID NO : 1757) of a native sequence PRO1107 cDNA 1757 is a clone designated herein as "DNA59606".

Figure 1758 shows the amino acid sequence (SEQ ID NO : 1758) derived from the coding sequence ( in Figure 1757.

Figure 1759 shows a nucleotide sequence (SEQ ID NO : 1759) of a native sequence PR083979 cDN, 1759 is a clone designated herein as "DNA328066".

Figure 1760 shows the amino acid sequence (SEQ ID NO : 1760) derived from the coding sequence ( in Figure 1759.

Figure 1761 shows a nucleotide sequence (SEQ ID NO : 1761) of a native sequence PR083980 cDN, 1761 is a clone designated herein as "DNA328067".

Figure 1762 shows the amino acid sequence (SEQ ID NO : 1762) derived from the coding sequence ( in Figure 1761.

Figure 1763 shows a nucleotide sequence (SEQ ID NO : 1763) of a native sequence PR083981 cDN 1763 is a clone designated herein as "DNA328068".

Figure 1764 shows the amino acid sequence (SEQ ID NO : 1764) derived from the coding sequence ( in Figure 1763.

Figure 1765 shows a nucleotide sequence (SEQ ID NO : 1765) of a native sequence cDNA, wherein : designated herein as "DNA161182".

Figure 1766 shows a nucleotide sequence (SEQ ID NO : 1766) of a native sequence PR0363 cDNA, \ is a clone designated herein as "DNA328069".

Figure 1767 shows the amino acid sequence (SEQ ID NO : 1767) derived from the coding sequence ( in Figure 1766.

Figure 1768 shows a nucleotide sequence (SEQ ID NO : 1768) of a native sequence PR083982 cDN, 1768 is a clone designated herein as "DNA328070".

Figure 1769 shows the amino acid sequence (SEQ ID NO : 1769) derived from the coding sequence ( in Figure 1768.

Figure 1770 shows a nucleotide sequence (SEQ ID NO : 1770) of a native sequence PRO83983 cDN, 1770 is a clone designated herein as "DNA328071".

Figure 1771 shows the amino acid sequence (SEQ ID NO : 1771) derived from the coding sequence in Figure 1770.

Figure 1772 shows a nucleotide sequence (SEQ ID NO : 1772) of a native sequence cDNA, wherein : designated herein as "DNA328072".

Figure 1773 shows a nucleotide sequence (SEQ ID NO : 1773) of a native sequence PRO83985 cDN 1773 is a clone designated herein as "DNA328073".

Figure 1774 shows the amino acid sequence (SEQ ID NO : 1774) derived from the coding sequence in Figure 1773.

Figure 1775 shows a nucleotide sequence (SEQ ID NO : 1775) of a native sequence PRO54700 cDN, 1775 is a clone designated herein as "DNA260948".

Figure 1776 shows the amino acid sequence (SEQ ID NO : 1776) derived from the coding sequence in Figure 1775.

Figure 1777 shows a nucleotide sequence (SEQ ID NO : 1777) of a native sequence cDNA, wherein : designated herein as "DNA328074".

Figure 1778 shows a nucleotide sequence (SEQ ID NO : 1778) of a native sequence PRO23594 cDN, 1778 is a clone designated herein as "DNA194202".

Figure 1779 shows the amino acid sequence (SEQ ID NO : 1779) derived from the coding sequence in Figure 1778.

Figure 1780 shows a nucleotide sequence (SEQ ID NO : 1780) of a native sequence cDNA, wherein : designated herein as "DNA328075".

Figure 1781 shows a nucleotide sequence (SEQ ID NO : 1781) of a native sequence PRO83988 cDN 1781 is a clone designated herein as "DNA328076".

Figure 1782 shows the amino acid sequence (SEQ ID NO : 1782) derived from the coding sequence in Figure 1781.

Figure 1783 shows a nucleotide sequence (SEQ ID NO : 1783) of a native sequence PRO83989 cDN 1783 is a clone designated herein as "DNA328077".

Figure 1784 shows the amino acid sequence (SEQ ID NO : 1784) derived from the coding sequence in Figure 1783.

Figure 1785 shows a nucleotide sequence (SEQ ID NO : 1785) of a native sequence PRO11946 cDN 1785 is a clone designated herein as "DNA151632".

Figure 1786 shows the amino acid sequence (SEQ ID NO : 1786) derived from the coding sequence in Figure 1785.

Figure 1787 shows a nucleotide sequence (SEQ ID NO : 1787) of a native sequence cDNA, wherein designated herein as "DNA195938".

Figure 1788 shows a nucleotide sequence (SEQ ID NO : 1788) of a native sequence PR083990 cDN. 1788 is a clone designated herein as "DNA328078".

Figure 1789 shows the amino acid sequence (SEQ ID NO : 1789) derived from the coding sequence in Figure 1788.

Figure 1790 shows a nucleotide sequence (SEQ ID NO : 1790) of a native sequence PR083991 cDN. 1790 is a clone designated herein as "DNA328079".

Figure 1791 shows the amino acid sequence (SEQ ID NO : 1791) derived from the coding sequence in Figure 1790.

Figure 1792 shows a nucleotide sequence (SEQ ID NO : 1792) of a native sequence cDNA, wherein designated herein as "DNA257517".

Figure 1793 shows a nucleotide sequence (SEQ ID NO : 1793) of a native sequence PR083992 cDN. 1793 is a clone designated herein as "DNA328080".

Figure 1794 shows the amino acid sequence (SEQ ID NO : 1794) derived from the coding sequence in Figure 1793.

Figure 1795 shows a nucleotide sequence (SEQ ID NO : 1795) of a native sequence PR083993 cDN. 1795 is a clone designated herein as "DNA328081".

Figure 1796 shows the amino acid sequence (SEQ ID NO : 1796) derived from the coding sequence in Figure 1795.

Figure 1797 shows a nucleotide sequence (SEQ ID NO : 1797) of a native sequence PR083994 cDN. 1797 is a clone designated herein as "DNA328082".

Figure 1798 shows the amino acid sequence (SEQ ID NO : 1798) derived from the coding sequence in Figure 1797.

Figure 1799 shows a nucleotide sequence (SEQ ID NO : 1799) of a native sequence PR083995 cDN. 1799 is a clone designated herein as "DNA328083".

Figure 1800 shows the amino acid sequence (SEQ ID NO : 1800) derived from the coding sequence in Figure 1799.

Figure 1801 shows a nucleotide sequence (SEQ ID NO : 1801) of a native sequence PR037611 cDN, 1801 is a clone designated herein as "DNA227148".

Figure 1802 shows the amino acid sequence (SEQ ID NO : 1802) derived from the coding sequence , in Figure 1801.

Figure 1803 shows a nucleotide sequence (SEQ ID NO : 1803) of a native sequence PR083996 cDN, 1803 is a clone designated herein as "DNA328084".

Figure 1804 shows the amino acid sequence (SEQ ID NO : 1804) derived from the coding sequence , in Figure 1803.

Figure 1805 shows a nucleotide sequence (SEQ ID NO : 1805) of a native sequence PR083997 cDN, 1805 is a clone designated herein as "DNA328085".

Figure 1806 shows the amino acid sequence (SEQ ID NO : 1806) derived from the coding sequence , in Figure 1805.

Figure 1807 shows a nucleotide sequence (SEQ ID NO : 1807) of a native sequence PR034934 cDN, 1807 is a clone designated herein as "DNA328086".

Figure 1808 shows the amino acid sequence (SEQ ID NO : 1808) derived from the coding sequence c in Figure 1807.

Figure 1809 shows a nucleotide sequence (SEQ ID NO : 1809) of a native sequence PRO83998 cDN 1809 is a clone designated herein as "DNA328087".

Figure 1810 shows the amino acid sequence (SEQ ID NO : 1810) derived from the coding sequence , in Figure 1809.

Figure 1811 shows a nucleotide sequence (SEQ ID NO : 1811) of a native sequence PRO83999 cDN 1811 is a clone designated herein as "DNA328088".

Figure 1812 shows the amino acid sequence (SEQ ID NO : 1812) derived from the coding sequence , in Figure 1811.

Figure 1813 shows a nucleotide sequence (SEQ ID NO : 1813) of a native sequence PR084000 cDN, 1813 is a clone designated herein as "DNA328089".

Figure 1814 shows the amino acid sequence (SEQ ID NO : 1814) derived from the coding sequence , in Figure 1813.

Figure 1815 shows a nucleotide sequence (SEQ ID NO : 1815) of a native sequence PRO84001 cDN 1815 is a clone designated herein as "DNA328090".

Figure 1816 shows the amino acid sequence (SEQ ID NO : 1816) derived from the coding sequence , in Figure 1815



Figure 1817 shows a nucleotide sequence (SEQ ID NO : 1817) of a native sequence PR084002 cDN, 1817 is a clone designated herein as "DNA328091".

Figure 1818 shows the amino acid sequence (SEQ ID NO : 1818) derived from the coding sequence in Figure 1817.

Figure 1819 shows a nucleotide sequence (SEQ ID NO : 1819) of a native sequence PR084003 cDN, 1819 is a clone designated herein as "DNA328092".

Figure 1820 shows the amino acid sequence (SEQ ID NO : 1820) derived from the coding sequence in Figure 1819.

Figure 1821 shows a nucleotide sequence (SEQ ID NO : 1821) of a native sequence PR037631 cDN, 1821 is a clone designated herein as "DNA227168".

Figure 1822 shows the amino acid sequence (SEQ ID NO : 1822) derived from the coding sequence in Figure 1821.

Figure 1823 shows a nucleotide sequence (SEQ ID NO : 1823) of a native sequence PR084004 cDN, 1823 is a clone designated herein as "DNA328093".

Figure 1824 shows the amino acid sequence (SEQ ID NO : 1824) derived from the coding sequence in Figure 1823.

Figure 1825 shows a nucleotide sequence (SEQ ID NO : 1825) of a native sequence PR084005 cDN, 1825 is a clone designated herein as "DNA328094".

Figure 1826 shows the amino acid sequence (SEQ ID NO : 1826) derived from the coding sequence in Figure 1825.

Figure 1827 shows a nucleotide sequence (SEQ ID NO : 1827) of a native sequence PR050404 cDN, 1827 is a clone designated herein as "DNA255334".

Figure 1828 shows the amino acid sequence (SEQ ID NO : 1828) derived from the coding sequence in Figure 1827.

Figure 1829 shows a nucleotide sequence (SEQ ID NO : 1829) of a native sequence PR084006 cDN, 1829 is a clone designated herein as "DNA328095".

Figure 1830 shows the amino acid sequence (SEQ ID NO : 1830) derived from the coding sequence in Figure 1829.

Figure 1831 shows a nucleotide sequence (SEQ ID NO : 1831) of a native sequence PR084007 cDN, 1831 is a clone designated herein as "DNA328096".

Figure 1832 shows the amino acid sequence (SEQ ID NO : 1832) derived from the coding sequence in Figure 1831.

Figure 1833 shows a nucleotide sequence (SEQ ID NO : 1833) of a native sequence PRO1192 cDNA 1833 is a clone designated herein as "DNA328097".

Figure 1834 shows the amino acid sequence (SEQ ID NO : 1834) derived from the coding sequence in Figure 1833.

Figure 1835 shows a nucleotide sequence (SEQ ID NO : 1835) of a native sequence PR084008 cDNA 1835 is a clone designated herein as "DNA328098".

Figure 1836 shows the amino acid sequence (SEQ ID NO : 1836) derived from the coding sequence in Figure 1835.

Figure 1837 shows a nucleotide sequence (SEQ ID NO : 1837) of a native sequence PR084009 cDNA 1837 is a clone designated herein as "DNA328099".

Figure 1838 shows the amino acid sequence (SEQ ID NO : 1838) derived from the coding sequence in Figure 1837.

Figure 1839 shows a nucleotide sequence (SEQ ID NO : 1839) of a native sequence PR084010 cDNA 1839 is a clone designated herein as "DNA328100".

Figure 1840 shows the amino acid sequence (SEQ ID NO : 1840) derived from the coding sequence in Figure 1839.

Figure 1841 shows a nucleotide sequence (SEQ ID NO : 1841) of a native sequence PR084011 cDNA 1841 is a clone designated herein as "DNA328101".

Figure 1842 shows the amino acid sequence (SEQ ID NO : 1842) derived from the coding sequence in Figure 1841.

Figure 1843 shows a nucleotide sequence (SEQ ID NO : 1843) of a native sequence PR084012 cDNA 1843 is a clone designated herein as "DNA328102".

Figure 1844 shows the amino acid sequence (SEQ ID NO : 1844) derived from the coding sequence in Figure 1843.

Figure 1845 shows a nucleotide sequence (SEQ ID NO : 1845) of a native sequence PR084013 cDNA 1845 is a clone designated herein as "DNA328103".

Figure 1846 shows the amino acid sequence (SEQ ID NO : 1846) derived from the coding sequence in Figure 1845.

Figure 1847 shows a nucleotide sequence (SEQ ID NO : 1847) of a native sequence PR084014 cDNA 1847 is a clone designated herein as "DNA328104".

Figure 1848 shows the amino acid sequence (SEQ ID NO : 1848) derived from the coding sequence in Figure 1847.

Figure 1849 shows a nucleotide sequence (SEQ ID NO : 1849) of a native sequence PRO84015 cDNA 1849 is a clone designated herein as "DNA328105".

Figure 1850 shows the amino acid sequence (SEQ ID NO : 1850) derived from the coding sequence in Figure 1849.

Figure 1851 shows a nucleotide sequence (SEQ ID NO : 1851) of a native sequence PRO19611 cDNA 1851 is a clone designated herein as "DNA328106".

Figure 1852 shows the amino acid sequence (SEQ ID NO : 1852) derived from the coding sequence in Figure 1851.

Figure 1853 shows a nucleotide sequence (SEQ ID NO : 1853) of a native sequence cDNA, where designated herein as "DNA195707".

Figure 1854 shows a nucleotide sequence (SEQ ID NO : 1854) of a native sequence cDNA "where designated herein as "DNA328107".

Figure 1855 shows a nucleotide sequence (SEQ ID NO : 1855) of a native sequence PRO84016 cDNA 1855 is a clone designated herein as "DNA328108".

Figure 1856 shows the amino acid sequence (SEQ ID NO : 1856) derived from the coding sequence in Figure 1855.

Figure 1857 shows a nucleotide sequence (SEQ ID NO : 1857) of a native sequence PRO84017 cDNA 1857 is a clone designated herein as "DNA328109".

Figure 1858 shows the amino acid sequence (SEQ ID NO : 1858) derived from the coding sequence in Figure 1857.

Figure 1859 shows a nucleotide sequence (SEQ ID NO : 1859) of a native sequence PRO84018 cDNA 1859 is a clone designated herein as "DNA328110".

Figure 1860 shows the amino acid sequence (SEQ ID NO : 1860) derived from the coding sequence in Figure 1859.

Figure 1861 shows a nucleotide sequence (SEQ ID NO : 1861) of a native sequence PRO4327 cDNA 1861 is a clone designated herein as "DNA328111".

Figure 1862 shows the amino acid sequence (SEQ ID NO : 1862) derived from the coding sequence in Figure 1861.

Figure 1863 shows a nucleotide sequence (SEQ ID NO : 1863) of a native sequence PRO80060 cDN, 1863 is a clone designated herein as "DNA271776".

Figure 1864 shows the amino acid sequence (SEQ ID NO : 1864) derived from the coding sequence, in Figure 1863.

Figure 1865 shows a nucleotide sequence (SEQ ID NO : 1865) of a native sequence cDNA, wherein : designated herein as "DNA328112".

Figure 1866 shows a nucleotide sequence (SEQ ID NO : 1866) of a native sequence PRO84020 cDN 1866 is a clone designated herein as "DNA328113".

Figure 1867 shows the amino acid sequence (SEQ ID NO : 1867) derived from the coding sequence, in Figure 1866.

Figure 1868 shows a nucleotide sequence (SEQ ID NO : 1868) of a native sequence PRO84021 cDN, 1868 is a clone designated herein as "DNA328114".

Figure 1869 shows the amino acid sequence (SEQ ID NO : 1869) derived from the coding sequence, in Figure 1868.

Figure 1870 shows a nucleotide sequence (SEQ ID NO : 1870) of a native sequence PRO84022 cDN 1870 is a clone designated herein as "DNA328115".

Figure 1871 shows the amino acid sequence (SEQ ID NO : 1871) derived from the coding sequence, in Figure 1870.

Figure 1872 shows a nucleotide sequence (SEQ ID NO : 1872) of a native sequence PRO84023 cDN, 1872 is a clone designated herein as "DNA328116".

Figure 1873 shows the amino acid sequence (SEQ ID NO : 1873) derived from the coding sequence, in Figure 1872.

Figure 1874 shows a nucleotide sequence (SEQ ID NO : 1874) of a native sequence cDNA, wherein : designated herein as "DNA256068".

Figure 1875 shows a nucleotide sequence (SEQ ID NO : 1875) of a native sequence PRO84024 cDN, 1875 is a clone designated herein as "DNA328117".

Figure 1876 shows the amino acid sequence (SEQ ID NO : 1876) derived from the coding sequence, in Figure 1875.

Figure 1877 shows a nucleotide sequence (SEQ ID NO : 1877) of a native sequence PRO84025 cDN, 1877 is a clone designated herein as "DNA328118".

Figure 1878 shows the amino acid sequence (SEQ ID NO : 1878) derived from the coding sequence, in Figure 1877.

Figure 1879 shows a nucleotide sequence (SEQ ID NO : 1879) of a native sequence PR084026 cl 1879 is a clone designated herein as "DNA328119".

Figure 1880 shows the amino acid sequence (SEQ ID NO : 1880) derived from the coding sequence in Figure 1879.

Figure 1881 shows a nucleotide sequence (SEQ ID NO : 1881) of a native sequence cDNA, where designated herein as "DNA328120".

Figure 1882 shows a nucleotide sequence (SEQ ID NO : 1882) of a native sequence PR084028 cl 1882 is a clone designated herein as "DNA328121".

Figure 1883 shows the amino acid sequence (SEQ ID NO : 1883) derived from the coding sequence in Figure 1882.

Figure 1884 shows a nucleotide sequence (SEQ ID NO : 1884) of a native sequence PR084029 cl 1884 is a clone designated herein as "DNA328122".

Figure 1885 shows the amino acid sequence (SEQ ID NO : 1885) derived from the coding sequence in Figure 1884.

Figure 1886 shows a nucleotide sequence (SEQ ID NO : 1886) of a native sequence PR084030 cl 1886 is a clone designated herein as "DNA328123".

Figure 1887 shows the amino acid sequence (SEQ ID NO : 1887) derived from the coding sequence in Figure 1886.

Figure 1888 shows a nucleotide sequence (SEQ ID NO : 1888) of a native sequence cDNA, where designated herein as "DNA328124".

Figure 1889 shows a nucleotide sequence (SEQ ID NO : 1889) of a native sequence PR084031 cl 1889 is a clone designated herein as "DNA328125".

Figure 1890 shows the amino acid sequence (SEQ ID NO : 1890) derived from the coding sequence in Figure 1889.

Figure 1891 shows a nucleotide sequence (SEQ ID NO : 1891) of a native sequence PR084032 cl 1891 is a clone designated herein as "DNA328126".

Figure 1892 shows the amino acid sequence (SEQ ID NO : 1892) derived from the coding sequence in Figure 1891.

Figure 1893 shows a nucleotide sequence (SEQ ID NO : 1893) of a native sequence PR084033 cl 1893 is a clone designated herein as "DNA328127".

Figure 1894 shows the amino acid sequence (SEQ ID NO : 1894) derived from the coding sequence in Figure 1893.

Figure 1895 shows a nucleotide sequence (SEQ ID NO : 1895) of a native sequence PR084034 cDN 1895 is a clone designated herein as "DNA328128".

Figure 1896 shows the amino acid sequence (SEQ ID NO : 1896) derived from the coding sequence in Figure 1895.

Figure 1897 shows a nucleotide sequence (SEQ ID NO : 1897) of a native sequence PR084035 cDN 1897 is a clone designated herein as "DNA328129".

Figure 1898 shows the amino acid sequence (SEQ ID NO : 1898) derived from the coding sequence in Figure 1897.

Figure 1899 shows a nucleotide sequence (SEQ ID NO : 1899) of a native sequence PR084036 cDN 1899 is a clone designated herein as "DNA328130".

Figure 1900 shows the amino acid sequence (SEQ ID NO : 1900) derived from the coding sequence in Figure 1899.

Figure 1901 shows a nucleotide sequence (SEQ ID NO : 1901) of a native sequence PR084037 cDN 1901 is a clone designated herein as "DNA328131".

Figure 1902 shows the amino acid sequence (SEQ ID NO : 1902) derived from the coding sequence in Figure 1901.

Figure 1903 shows a nucleotide sequence (SEQ ID NO : 1903) of a native sequence PR084038 cDN 1903 is a clone designated herein as "DNA328132".

Figure 1904 shows the amino acid sequence (SEQ ID NO : 1904) derived from the coding sequence in Figure 1903.

Figure 1905 shows a nucleotide sequence (SEQ ID NO : 1905) of a native sequence PRO84039 cDN 1905 is a clone designated herein as "DNA328133".

Figure 1906 shows the amino acid sequence (SEQ ID NO : 1906) derived from the coding sequence in Figure 1905.

Figure 1907 shows a nucleotide sequence (SEQ ID NO : 1907) of a native sequence PRO84040 cDN 1907 is a clone designated herein as "DNA328134".

Figure 1908 shows the amino acid sequence (SEQ ID NO : 1908) derived from the coding sequence in Figure 1907.

Figure 1909 shows a nucleotide sequence (SEQ ID NO : 1909) of a native sequence PRO84041 cDN 1909 is a clone designated herein as "DNA328135".

Figure 1910 shows the amino acid sequence (SEQ ID NO : 1910) derived from the coding sequence in Figure 1909.

Figure 1911 shows a nucleotide sequence (SEQ ID NO : 1911) of a native sequence PR084082 cDN 1911 is a clone designated herein as "DNA328136".

Figure 1912 shows the amino acid sequence (SEQ ID NO : 1912) derived from the coding sequence in Figure 1911.

Figure 1913 shows a nucleotide sequence (SEQ ID NO : 1913) of a native sequence PRQ45876 cDN 1913 is a clone designated herein as "DNA210491".

Figure 1914 shows the amino acid sequence (SEQ ID NO : 1914) derived from the coding sequence in Figure 1913.

Figure 1915 shows a nucleotide sequence (SEQ ID NO : 1915) of a native sequence PR084043 cDN 1915 is a clone designated herein as "DNA328137".

Figure 1916 shows the amino acid sequence (SEQ ID NO : 1916) derived from the coding sequence in Figure 1915.

Figure 1917 shows a nucleotide sequence (SEQ ID NO : 1917) of a native sequence PR084044 cDN 1917 is a clone designated herein as "DNA328138".

Figure 1918 shows the amino acid sequence (SEQ ID NO : 1918) derived from the coding sequence in Figure 1917.

Figure 1919 shows a nucleotide sequence (SEQ ID NO : 1919) of a native sequence PR06006 cDNA is a clone designated herein as "DNA328139".

Figure 1920 shows the amino acid sequence (SEQ ID NO : 1920) derived from the coding sequence in Figure 1919.

Figure 1921 shows a nucleotide sequence (SEQ ID NO : 1921) of a native sequence PR084045 cDN 1921 is a clone designated herein as "DNA328140".

Figure 1922 shows the amino acid sequence (SEQ ID NO : 1922) derived from the coding sequence in Figure 1921.

Figure 1923 shows a nucleotide sequence (SEQ ID NO : 1923) of a native sequence PR084046 cDN 1923 is a clone designated herein as "DNA328141".

Figure 1924 shows the amino acid sequence (SEQ ID NO : 1924) derived from the coding sequence in Figure 1923.

Figure 1925 shows a nucleotide sequence (SEQ ID NO : 1925) of a native sequence PR084047 cDN,  
1925 is a clone designated herein as "DNA328142".

Figure 1926 shows the amino acid sequence (SEQ ID NO : 1926) derived from the coding sequence c  
in Figure 1925.

Figure 1927 shows a nucleotide sequence (SEQ ID NO : 1927) of a native sequence PRO84048 cDN  
1927 is a clone designated herein as "DNA328143".

Figure 1928 shows the amino acid sequence (SEQ ID NO : 1928) derived from the coding sequence c  
in Figure 1927.

Figure 1929 shows a nucleotide sequence (SEQ ID NO : 1929) of a native sequence PRO84049 cDN  
1929 is a clone designated herein as "DNA328144".

Figure 1930 shows the amino acid sequence (SEQ ID NO : 1930) derived from the coding sequence c  
in Figure 1929.

Figure 1931 shows a nucleotide sequence (SEQ ID NO : 1931) of a native sequence PR084050 cDN,  
1931 is a clone designated herein as "DNA328145".

Figure 1932 shows the amino acid sequence (SEQ ID NO : 1932) derived from the coding sequence c  
in Figure 1931.

Figure 1933 shows a nucleotide sequence (SEQ ID NO : 1933) of a native sequence PR084051 cDN,  
1933 is a clone designated herein as "DNA328146".

Figure 1934 shows the amino acid sequence (SEQ ID NO : 1934) derived from the coding sequence c  
in Figure 1933.

Figure 1935 shows a nucleotide sequence (SEQ ID NO : 1935) of a native sequence PR084052 cDN,  
1935 is a clone designated herein as "DNA328147".

Figure 1936 shows the amino acid sequence (SEQ ID NO : 1936) derived from the coding sequence c  
in Figure 1935.

Figure 1937 shows a nucleotide sequence (SEQ ID NO : 1937) of a native sequence PR084053 cDN,  
1937 is a clone designated herein as "DNA328148".

Figure 1938 shows the amino acid sequence (SEQ ID NO : 1938) derived from the coding sequence c  
in Figure 1937.

Figure 1939 shows a nucleotide sequence (SEQ ID NO : 1939) of a native sequence PRO84054 cDN  
1939 is a clone designated herein as "DNA328149".

Figure 1940 shows the amino acid sequence (SEQ ID NO : 1940) derived from the coding sequence c  
in Figure 1939.



Figure 1941 shows a nucleotide sequence (SEQ ID NO : 1941) of a native sequence PRO1343 cDNA 1941 is a clone designated herein as "DNA66675".

Figure 1942 shows the amino acid sequence (SEQ ID NO : 1942) derived from the coding sequence in Figure 1941.

Figure 1943 shows a nucleotide sequence (SEQ ID NO : 1943) of a native sequence PR084055 cDN, 1943 is a clone designated herein as "DNA328150".

Figure 1944 shows the amino acid sequence (SEQ ID NO : 1944) derived from the coding sequence in Figure 1943.

Figure 1945 shows a nucleotide sequence (SEQ ID NO : 1945) of a native sequence PR084056 cDN, 1945 is a clone designated herein as "DNA328151".

Figure 1946 shows the amino acid sequence (SEQ ID NO : 1946) derived from the coding sequence in Figure 1945.

Figure 1947 shows a nucleotide sequence (SEQ ID NO : 1947) of a native sequence PRO84057 cDN 1947 is a clone designated herein as "DNA328152".

Figure 1948 shows the amino acid sequence (SEQ ID NO : 1948) derived from the coding sequence in Figure 1947.

Figure 1949 shows a nucleotide sequence (SEQ ID NO : 1949) of a native sequence cDNA, wherein : designated herein as "DNA257872".

Figure 1950 shows a nucleotide sequence (SEQ ID NO : 1950) of a native sequence PR084058 cDN, 1950 is a clone designated herein as "DNA328153".

Figure 1951 shows the amino acid sequence (SEQ ID NO : 1951) derived from the coding sequence in Figure 1950.

Figure 1952 shows a nucleotide sequence (SEQ ID NO : 1952) of a native sequence PRO84059 cDN 1952 is a clone designated herein as "DNA328154".

Figure 1953 shows the amino acid sequence (SEQ ID NO : 1953) derived from the coding sequence in Figure 1952.

Figure 1954 shows a nucleotide sequence (SEQ ID NO : 1954) of a native sequence PRO84060 cDN 1954 is a clone designated herein as "DNA328155".

Figure 1955 shows the amino acid sequence (SEQ ID NO : 1955) derived from the coding sequence in Figure 1954.

Figure 1956 shows a nucleotide sequence (SEQ ID NO : 1956) of a native sequence PRO84061. 1956 is a clone designated herein as "DNA328156".

Figure 1957 shows the amino acid sequence (SEQ ID NO : 1957) derived from the coding sequence in Figure 1956.

Figure 1958 shows a nucleotide sequence (SEQ ID NO : 1958) of a native sequence PRO84062. 1958 is a clone designated herein as "DNA328157".

Figure 1959 shows the amino acid sequence (SEQ ID NO : 1959) derived from the coding sequence in Figure 1958.

Figure 1960 shows a nucleotide sequence (SEQ ID NO : 1960) of a native sequence PRO84063. 1960 is a clone designated herein as "DNA328158".

Figure 1961 shows the amino acid sequence (SEQ ID NO : 1961) derived from the coding sequence in Figure 1960.

Figure 1962 shows a nucleotide sequence (SEQ ID NO : 1962) of a native sequence cDNA, which is designated herein as "DNA328159".

Figure 1963 shows a nucleotide sequence (SEQ ID NO : 1963) of a native sequence PRO84064. 1963 is a clone designated herein as "DNA328160".

Figure 1964 shows the amino acid sequence (SEQ ID NO : 1964) derived from the coding sequence in Figure 1963.

Figure 1965 shows a nucleotide sequence (SEQ ID NO : 1965) of a native sequence PRO84065. 1965 is a clone designated herein as "DNA328161".

Figure 1966 shows the amino acid sequence (SEQ ID NO : 1966) derived from the coding sequence in Figure 1965.

Figure 1967 shows a nucleotide sequence (SEQ ID NO : 1967) of a native sequence PRO84066. 1967 is a clone designated herein as "DNA328162".

Figure 1968 shows the amino acid sequence (SEQ ID NO : 1968) derived from the coding sequence in Figure 1967.

Figure 1969 shows a nucleotide sequence (SEQ ID NO : 1969) of a native sequence PRO84067. 1969 is a clone designated herein as "DNA328163".

Figure 1970 shows the amino acid sequence (SEQ ID NO : 1970) derived from the coding sequence in Figure 1969.

Figure 1971 shows a nucleotide sequence (SEQ ID NO : 1971) of a native sequence PRO84068. 1971 is a clone designated herein as "DNA328164".

Figure 1972 shows the amino acid sequence (SEQ ID NO : 1972) derived from the coding sequence in Figure 1971.

Figure 1973 shows a nucleotide sequence (SEQ ID NO : 1973) of a native sequence PRO38220 cDN 1973 is a clone designated herein as "DNA328165".

Figure 1974 shows the amino acid sequence (SEQ ID NO : 1974) derived from the coding sequence in Figure 1973.

Figure 1975 shows a nucleotide sequence (SEQ ID NO : 1975) of a native sequence PRO84069 cDN 1975 is a clone designated herein as "DNA328166".

Figure 1976 shows the amino acid sequence (SEQ ID NO : 1976) derived from the coding sequence in Figure 1975.

Figure 1977 shows a nucleotide sequence (SEQ ID NO : 1977) of a native sequence PRO84070 cDN 1977 is a clone designated herein as "DNA328167".

Figure 1978 shows the amino acid sequence (SEQ ID NO : 1978) derived from the coding sequence in Figure 1977.

Figure 1979 shows a nucleotide sequence (SEQ ID NO : 1979) of a native sequence PRO84071 cDN 1979 is a clone designated herein as "DNA328168".

Figure 1980 shows the amino acid sequence (SEQ ID NO : 1980) derived from the coding sequence in Figure 1979.

Figure 1981 shows a nucleotide sequence (SEQ ID NO : 1981) of a native sequence PRO84072 cDN 1981 is a clone designated herein as "DNA328169".

Figure 1982 shows the amino acid sequence (SEQ ID NO : 1982) derived from the coding sequence in Figure 1981.

Figure 1983 shows a nucleotide sequence (SEQ ID NO : 1983) of a native sequence PRO84073 cDN 1983 is a clone designated herein as "DNA328170".

Figure 1984 shows the amino acid sequence (SEQ ID NO : 1984) derived from the coding sequence in Figure 1983.

Figure 1985 shows a nucleotide sequence (SEQ ID NO : 1985) of a native sequence PRO84074 cDN 1985 is a clone designated herein as "DNA328171".

Figure 1986 shows the amino acid sequence (SEQ ID NO : 1986) derived from the coding sequence in Figure 1985.

Figure 1987 shows a nucleotide sequence (SEQ ID NO : 1987) of a native sequence PRO84075 1987 is a clone designated herein as "DNA328172".

Figure 1988 shows the amino acid sequence (SEQ ID NO : 1988) derived from the coding sequence in Figure 1987.

Figure 1989 shows a nucleotide sequence (SEQ ID NO : 1989) of a native sequence PRO84076 1989 is a clone designated herein as "DNA328173".

Figure 1990 shows the amino acid sequence (SEQ ID NO : 1990) derived from the coding sequence in Figure 1989.

Figure 1991 shows a nucleotide sequence (SEQ ID NO : 1991) of a native sequence PRO84077 1991 is a clone designated herein as "DNA328174".

Figure 1992 shows the amino acid sequence (SEQ ID NO : 1992) derived from the coding sequence in Figure 1991.

Figure 1993 shows a nucleotide sequence (SEQ ID NO : 1993) of a native sequence PRO84078 1993 is a clone designated herein as "DNA328175".

Figure 1994 shows the amino acid sequence (SEQ ID NO : 1994) derived from the coding sequence in Figure 1993.

Figure 1995 shows a nucleotide sequence (SEQ ID NO:1995) of a native sequence PRO84079 c is a clone designated herein as "DNA328176".

Figure 1996 shows the amino acid sequence (SEQ ID NO : 1996) derived from the coding sequence in Figure 1995.

Figure 1997 shows a nucleotide sequence (SEQ ID NO : 1997) of a native sequence PRO84080 1997 is a clone designated herein as "DNA328177".

Figure 1998 shows the amino acid sequence (SEQ ID NO : 1998) derived from the coding sequence in Figure 1997.

Figure 1999 shows a nucleotide sequence (SEQ ID NO : 1999) of a native sequence PRO84081 1999 is a clone designated herein as "DNA328178".

Figure 2000 shows the amino acid sequence (SEQ ID NO : 2000) derived from the coding sequence in Figure 1999.

Figure 2001 shows a nucleotide sequence (SEQ ID NO : 2001) of a native sequence PRO84082 2001 is a clone designated herein as "DNA328179".

Figure 2002 shows the amino acid sequence (SEQ ID NO : 2002) derived from the coding sequence in Figure 2001.

Figure 2003 shows a nucleotide sequence (SEQ ID NO : 2003) of a native sequence PRO84083 cDN, 2003 is a clone designated herein as "DNA328180".

Figure 2004 shows the amino acid sequence (SEQ ID NO : 2004) derived from the coding sequence, in Figure 2003.

Figure 2005 shows a nucleotide sequence (SEQ ID NO : 2005) of a native sequence PRO84084 cDN, 2005 is a clone designated herein as "DNA328181".

Figure 2006 shows the amino acid sequence (SEQ ID NO : 2006) derived from the coding sequence, in Figure 2005.

Figure 2007 shows a nucleotide sequence (SEQ ID NO : 2007) of a native sequence PRO84085 cDN, 2007 is a clone designated herein as "DNA328182".

Figure 2008 shows the amino acid sequence (SEQ ID NO : 2008) derived from the coding sequence, in Figure 2007.

Figure 2009 shows a nucleotide sequence (SEQ ID NO : 2009) of a native sequence PRO84086 cDN, 2009 is a clone designated herein as "DNA328183".

Figure 2010 shows the amino acid sequence (SEQ ID NO : 2010) derived from the coding sequence, in Figure 2009.

Figure 2011 shows a nucleotide sequence (SEQ ID NO : 2011) of a native sequence PRO84087 cDN, 2011 is a clone designated herein as "DNA328184".

Figure 2012 shows the amino acid sequence (SEQ ID NO : 2012) derived from the coding sequence, in Figure 2011.

Figure 2013 shows a nucleotide sequence (SEQ ID NO : 2013) of a native sequence PRO52486 cDN, 2013 is a clone designated herein as "DNA257959".

Figure 2014 shows the amino acid sequence (SEQ ID NO : 2014) derived from the coding sequence, in Figure 2013.

Figure 2015 shows a nucleotide sequence (SEQ ID NO : 2015) of a native sequence PRO84088 cDN, 2015 is a clone designated herein as "DNA328185".

Figure 2016 shows the amino acid sequence (SEQ ID NO : 2016) derived from the coding sequence, in Figure 2015.

Figure 2017 shows a nucleotide sequence (SEQ ID NO : 2017) of a native sequence PRO84089 cDN, 2017 is a clone designated herein as "DNA328186".

Figure 2018 shows the amino acid sequence (SEQ ID NO : 2018) derived from the coding sequence in Figure 2017.

Figure 2019 shows a nucleotide sequence (SEQ ID NO : 2019) of a native sequence PR084090 cDN 2019 is a clone designated herein as "DNA328187".

Figure 2020 shows the amino acid sequence (SEQ ID NO : 2020) derived from the coding sequence in Figure 2019.

Figure 2021 shows a nucleotide sequence (SEQ ID NO : 2021) of a native sequence PR084091 cDN 2021 is a clone designated herein as "DNA328188".

Figure 2022 shows the amino acid sequence (SEQ ID NO : 2022) derived from the coding sequence in Figure 2021.

Figure 2023 shows a nucleotide sequence (SEQ ID NO : 2023) of a native sequence PR084092 cDN 2023 is a clone designated herein as "DNA328189".

Figure 2024 shows the amino acid sequence (SEQ ID NO : 2024) derived from the coding sequence in Figure 2023.

Figure 2025 shows a nucleotide sequence (SEQ ID NO : 2025) of a native sequence PR084093 cDN 2025 is a clone designated herein as "DNA328190".

Figure 2026 shows the amino acid sequence (SEQ ID NO : 2026) derived from the coding sequence in Figure 2025.

Figure 2027 shows a nucleotide sequence (SEQ ID NO : 2027) of a native sequence PR084094 cDN 2027 is a clone designated herein as "DNA328191".

Figure 2028 shows the amino acid sequence (SEQ ID NO : 2028) derived from the coding sequence in Figure 2027.

Figure 2029 shows a nucleotide sequence (SEQ ID NO : 2029) of a native sequence PR084095 cDN 2029 is a clone designated herein as "DNA328192".

Figure 2030 shows the amino acid sequence (SEQ ID NO : 2030) derived from the coding sequence in Figure 2029.

Figure 2031 shows a nucleotide sequence (SEQ ID NO : 2031) of a native sequence PR084096 cDN 2031 is a clone designated herein as "DNA328193".

Figure 2032 shows the amino acid sequence (SEQ ID NO : 2032) derived from the coding sequence in Figure 2031.

Figure 2033 shows a nucleotide sequence (SEQ ID NO : 2033) of a native sequence PR084097 cDN 2033 is a clone designated herein as "DNA328194".

Figure 2034 shows the amino acid sequence (SEQ ID NO : 2034) derived from the coding sequence in Figure 2033.

Figure 2035 shows a nucleotide sequence (SEQ ID NO : 2035) of a native sequence PRO84098 c2035 is a clone designated herein as "DNA328195".

Figure 2036 shows the amino acid sequence (SEQ ID NO : 2036) derived from the coding sequence in Figure 2035.

Figure 2037 shows a nucleotide sequence (SEQ ID NO : 2037) of a native sequence PR084099 c2037 is a clone designated herein as "DNA328196".

Figure 2038 shows the amino acid sequence (SEQ ID NO : 2038) derived from the coding sequence in Figure 2037.

Figure 2039 shows a nucleotide sequence (SEQ ID NO : 2039) of a native sequence PRO84100 c2039 is a clone designated herein as "DNA328197".

Figure 2040 shows the amino acid sequence (SEQ ID NO : 2040) derived from the coding sequence in Figure 2039.

Figure 2041 shows a nucleotide sequence (SEQ ID NO : 2041) of a native sequence PRO84101 c2041 is a clone designated herein as "DNA328198".

Figure 2042 shows the amino acid sequence (SEQ ID NO : 2042) derived from the coding sequence in Figure 2041.

Figure 2043 shows a nucleotide sequence (SEQ ID NO : 2043) of a native sequence PRO84102 c2043 is a clone designated herein as "DNA328199".

Figure 2044 shows the amino acid sequence (SEQ ID NO : 2044) derived from the coding sequence in Figure 2043.

Figure 2045 shows a nucleotide sequence (SEQ ID NO : 2045) of a native sequence PRO1274 cD2045 is a clone designated herein as "DNA64889".

Figure 2046 shows the amino acid sequence (SEQ ID NO : 2046) derived from the coding sequence in Figure 2045.

Figure 2047 shows a nucleotide sequence (SEQ ID NO : 2047) of a native sequence PRO84103 c2047 is a clone designated herein as "DNA328200".

Figure 2048 shows the amino acid sequence (SEQ ID NO : 2048) derived from the coding sequence in Figure 2047.

Figure 2049 shows a nucleotide sequence (SEQ ID NO : 2049) of a native sequence PRO84104 2049 is a clone designated herein as "DNA328201".

Figure 2050 shows the amino acid sequence (SEQ ID NO : 2050) derived from the coding sequence in Figure 2049.

Figure 2051 shows a nucleotide sequence (SEQ ID NO : 2051) of a native sequence PR069126, 2051 is a clone designated herein as "DNA285363".

Figure 2052 shows the amino acid sequence (SEQ ID NO : 5052) derived from the coding sequence in Figure 2051., Figure 2053 shows a nucleotide sequence (SEQ ID NO : 2053) of a native sequence SEQ ID NO : 2053 is a clone designated herein as "DNA328202".

Figure 2054 shows the amino acid sequence (SEQ ID NO : 2054) derived from the coding sequence in Figure 2053.

Figure 2055 shows a nucleotide sequence (SEQ ID NO : 2055) of a native sequence PRO84106 2055 is a clone designated herein as "DNA328203".

Figure 2056 shows the amino acid sequence (SEQ ID NO : 2056) derived from the coding sequence in Figure 2055.

Figure 2057 shows a nucleotide sequence (SEQ ID NO : 2057) of a native sequence PR084107, 2057 is a clone designated herein as "DNA328204".

Figure 2058 shows the amino acid sequence (SEQ ID NO : 2058) derived from the coding sequence in Figure 2057.

Figure 2059 shows a nucleotide sequence (SEQ ID NO : 2059) of a native sequence PR084108, 2059 is a clone designated herein as "DNA328205".

Figure 2060 shows the amino acid sequence (SEQ ID NO : 2060) derived from the coding sequence in Figure 2059.

Figure 2061 shows a nucleotide sequence (SEQ ID NO : 2061) of a native sequence PR084109, 2061 is a clone designated herein as "DNA328206".

Figure 2062 shows the amino acid sequence (SEQ ID NO : 2062) derived from the coding sequence in Figure 2061.

Figure 2063 shows a nucleotide sequence (SEQ ID NO : 2063) of a native sequence PR084110, 2063 is a clone designated herein as "DNA328207".

Figure 2064 shows the amino acid sequence (SEQ ID NO : 2064) derived from the coding sequence in Figure 2063.

Figure 2065 shows a nucleotide sequence (SEQ ID NO : 2065) of a native sequence PR084111,



2065 is a clone designated herein as "DNA328208".

Figure 2066 shows the amino acid sequence (SEQ ID NO : 2066) derived from the coding sequence in Figure 2065.

Figure 2067 shows a nucleotide sequence (SEQ ID NO : 2067) of a native sequence PRO84112 cl 2067 is a clone designated herein as "DNA328209".

Figure 2068 shows the amino acid sequence (SEQ ID NO : 2068) derived from the coding sequence in Figure 2067.

Figure 2069 shows a nucleotide sequence (SEQ ID NO : 2069) of a native sequence PRO84113 cl 2069 is a clone designated herein as "DNA328210".

Figure 2070 shows the amino acid sequence (SEQ ID NO : 2070) derived from the coding sequence in Figure.

Figure 2071 shows a nucleotide sequence (SEQ ID NO : 2071) of a native sequence PRO84114 cl 2071 is a clone designated herein as "DNA328211".

Figure 2072 shows the amino acid sequence (SEQ ID NO : 2072) derived from the coding sequence in Figure 2071.

Figure 2073 shows a nucleotide sequence (SEQ ID NO : 2073) of a native sequence PRO84115 cl 2073 is a clone designated herein as "DNA328212".

Figure 2074 shows the amino acid sequence (SEQ ID NO : 2074) derived from the coding sequence in Figure 2073.

Figure 2075 shows a nucleotide sequence (SEQ ID NO : 2075) of a native sequence PRO84116 cl 2075 is a clone designated herein as "DNA328213".

Figure 2076 shows the amino acid sequence (SEQ ID NO : 2076) derived from the coding sequence in Figure 2075.

Figure 2077 shows a nucleotide sequence (SEQ ID NO : 2077) of a native sequence PRO84117 cl 2077 is a clone designated herein as "DNA328214".

Figure 2078 shows the amino acid sequence (SEQ ID NO : 2078) derived from the coding sequence in Figure 2077.

Figure 2079 shows a nucleotide sequence (SEQ ID NO : 2079) of a native sequence PRO84118 cl 2079 is a clone designated herein as "DNA328215".

Figure 2080 shows the amino acid sequence (SEQ ID NO : 2080) derived from the coding sequence in Figure 2079.

Figure 2081 shows a nucleotide sequence (SEQ ID NO : 2081) of a native sequence PRO84119 cl 2081 is a clone designated herein as "DNA328216".

Figure 2082 shows the amino acid sequence (SEQ ID NO : 2082) derived from the coding sequence in Figure 2081.

Figure 2083 shows a nucleotide sequence (SEQ ID NO : 2083) of a native sequence PRO84120 cl 2083 is a clone designated herein as "DNA328217".

Figure 2084 shows the amino acid sequence (SEQ ID NO : 2084) derived from the coding sequence in Figure 2083.

Figure 2085 shows a nucleotide sequence (SEQ ID NO : 2085) of a native sequence PRO84121 cl 2085 is a clone designated herein as "DNA328218".

Figure 2086 shows the amino acid sequence (SEQ ID NO : 2086) derived from the coding sequence in Figure 2085.

Figure 2087 shows a nucleotide sequence (SEQ ID NO : 2087) of a native sequence PRO84122 cl 2087 is a clone designated herein as "DNA328219".

Figure 2088 shows the amino acid sequence (SEQ ID NO : 2088) derived from the coding sequence in Figure 2087.

Figure 2089 shows a nucleotide sequence (SEQ ID NO : 2089) of a native sequence PRO84123 cl 2089 is a clone designated herein as "DNA328220".

Figure 2090 shows the amino acid sequence (SEQ ID NO : 2090) derived from the coding sequence in Figure 2089.

Figure 2091 shows a nucleotide sequence (SEQ ID NO : 2091) of a native sequence PRO84124 cl 2091 is a clone designated herein as "DNA328221".

Figure 2092 shows the amino acid sequence (SEQ ID NO : 2092) derived from the coding sequence in Figure 2091.

Figure 2093 shows a nucleotide sequence (SEQ ID NO : 2093) of a native sequence PRO84125 cl 2093 is a clone designated herein as "DNA328222".

Figure 2094 shows the amino acid sequence (SEQ ID NO : 2094) derived from the coding sequence in Figure 2093.

Figure 2095 shows a nucleotide sequence (SEQ ID NO : 2095) of a native sequence PRO84126 cl 2095 is a clone designated herein as "DNA328223".

Figure 2096 shows the amino acid sequence (SEQ ID NO : 2096) derived from the coding sequence in Figure 2095.

in Figure 2095.

Figure 2097 shows a nucleotide sequence (SEQ ID NO : 2097) of a native sequence PRO23265 cDN, 2097 is a clone designated herein as "DNA176718".

Figure 2098 shows the amino acid sequence (SEQ ID NO : 2098) derived from the coding sequence , in Figure 2097.

Figure 2099 shows a nucleotide sequence (SEQ ID NO : 2099) of a native sequence PRO84127 cDN 2099 is a clone designated herein as "DNA328224".

Figure 2100 shows the amino acid sequence (SEQ ID NO : 2100) derived from the coding sequence , in Figure 2099.

Figure 2101 shows a nucleotide sequence (SEQ ID NO : 2101) of a native sequence PRO84128 cDN, 2101 is a clone designated herein as "DNA328225".

Figure 2102 shows the amino acid sequence (SEQ ID NO : 2102) derived from the coding sequence , in Figure 2101.

Figure 2103 shows a nucleotide sequence (SEQ ID NO : 2103) of a native sequence PRO84129 cDN, 2103 is a clone designated herein as "DNA328226".

Figure 2104 shows the amino acid sequence (SEQ ID NO : 2104) derived from the coding sequence , in Figure 2103.

Figure 2105 shows a nucleotide sequence (SEQ ID NO : 2105) of a native sequence PRO84130 cDN 2105 is a clone designated herein as "DNA328227".

Figure 2106 shows the amino acid sequence (SEQ ID NO : 2106) derived from the coding sequence , in Figure 2105.

Figure 2107 shows a nucleotide sequence (SEQ ID NO : 2107) of a native sequence PRO84131 cDN 2107 is a clone designated herein as "DNA328228".

Figure 2108 shows the amino acid sequence (SEQ ID NO : 2108) derived from the coding sequence , in Figure 2107.

Figure 2109 shows a nucleotide sequence (SEQ ID NO : 2109) of a native sequence PRO84132 cDN 2109 is a clone designated herein as "DNA328229".

Figure 2110 shows the amino acid sequence (SEQ ID NO : 2110) derived from the coding sequence , in Figure 2109.

Figure 2111 shows a nucleotide sequence (SEQ ID NO : 2111) of a native sequence PRO84133 cDN 2111 is a clone designated herein as "DNA328230".

Figure 2112 shows the amino acid sequence (SEQ ID NO : 2112) derived from the coding sequence in Figure 2111.

Figure 2113 shows a nucleotide sequence (SEQ ID NO : 2113) of a native sequence PRO84134 c1 2113 is a clone designated herein as "DNA328231".

Figure 2114 shows the amino acid sequence (SEQ ID NO : 2114) derived from the coding sequence in Figure 2113.

Figure 2115 shows a nucleotide sequence (SEQ ID NO : 2115) of a native sequence PRO84135 c1 2115 is a clone designated herein as "DNA328232".

Figure 2116 shows the amino acid sequence (SEQ ID NO : 2116) derived from the coding sequence in Figure 2115.

Figure 2117 shows a nucleotide sequence (SEQ ID NO : 2117) of a native sequence PRO84136 c1 2117 is a clone designated herein as "DNA328233".

Figure 2118 shows the amino acid sequence (SEQ ID NO : 2118) derived from the coding sequence in Figure 2117.

Figure 2119 shows a nucleotide sequence (SEQ ID NO : 2119) of a native sequence PRO84137 c1 2119 is a clone designated herein as "DNA328234". t Figure 2120 shows the amino acid sequence from the coding sequence of SEQ ID NO : 2119 shown in Figure 2119.

Figure 2121 shows a nucleotide sequence (SEQ ID NO : 2121) of a native sequence PRO84138 c1 2121 is a clone designated herein as "DNA328235".

Figure 2122 shows the amino acid sequence (SEQ ID NO : 2122) derived from the coding sequence in Figure 2121.

Figure 2123 shows a nucleotide sequence (SEQ ID NO : 2123) of a native sequence PRO84139 c1 2123 is a clone designated herein as "DNA328236".

Figure 2124 shows the amino acid sequence (SEQ ID NO : 2124) derived from the coding sequence in Figure 2123.

Figure 2125 shows a nucleotide sequence (SEQ ID NO : 2125) of a native sequence PRO84140 c1 2125 is a clone designated herein as "DNA328237".

Figure 2126 shows the amino acid sequence (SEQ ID NO : 2126) derived from the coding sequence in Figure 2125.

Figure 2127 shows a nucleotide sequence (SEQ ID NO : 2127) of a native sequence PRO84141 c1 2127 is a clone designated herein as "DNA328238".

Figure 2128 shows the amino acid sequence (SEQ ID NO : 2128) derived from the coding sequence in Figure 2127.

Figure 2129 shows a nucleotide sequence (SEQ ID NO : 2129) of a native sequence PRO84142 2129 is a clone designated herein as "DNA328239".

Figure 2130 shows the amino acid sequence (SEQ ID NO : 2130) derived from the coding sequence in Figure 2129.

Figure 2131 shows a nucleotide sequence (SEQ ID NO : 2131) of a native sequence PRO84143 c 2131 is a clone designated herein as "DNA328240".

Figure 2132 shows the amino acid sequence (SEQ ID NO : 2132) derived from the coding sequence in Figure 2131.

Figure 2133 shows a nucleotide sequence (SEQ ID NO : 2133) of a native sequence PRO84144 , 2133 is a clone designated herein as "DNA328241".

Figure 2134 shows the amino acid sequence (SEQ ID NO : 2134) derived from the coding sequence in Figure 2133.

Figure 2135 shows a nucleotide sequence (SEQ ID NO : 2135) of a native sequence PRO84145 2135 is a clone designated herein as "DNA328242".

Figure 2136 shows the amino acid sequence (SEQ ID NO : 2136) derived from the coding sequence in Figure 2135.

Figure 2137 shows a nucleotide sequence (SEQ ID NO : 2137) of a native sequence cDNA, where designated herein as "DNA328243".

Figure 2138 shows a nucleotide sequence (SEQ ID NO : 2138) of a native sequence PRO1889 c 2138 is a clone designated herein as "DNA77623".

Figure 2139 shows the amino acid sequence (SEQ ID NO : 2139) derived from the coding sequence in Figure 2138.

Figure 2140 shows a nucleotide sequence (SEQ ID NO : 2140) of a native sequence PRO1918 c 2140 is a clone designated herein as "DNA328244".

Figure 2141 shows the amino acid sequence (SEQ ID NO : 2141) derived from the coding sequence in Figure 2140.

Figure 2142 shows a nucleotide sequence (SEQ ID NO : 2142) of a native sequence PRO84146 , 2142 is a clone designated herein as "DNA328245".

Figure 2143 shows the amino acid sequence (SEQ ID NO : 2143) derived from the coding sequence in Figure 2142.

Figure 2144 shows a nucleotide sequence (SEQ ID NO : 2144) of a native sequence PRO83476 cDNA, where 2144 is a clone designated herein as "DNA327201".

Figure 2145 shows the amino acid sequence (SEQ ID NO : 2145) derived from the coding sequence in Figure 2144.

Figure 2146 shows a nucleotide sequence (SEQ ID NO : 2146) of a native sequence cDNA, where designated herein as "DNA328246".

Figure 2147 shows a nucleotide sequence (SEQ ID NO : 2147) of a native sequence cDNA, where designated herein as "DNA328247".

Figure 2148 shows a nucleotide sequence (SEQ ID NO : 2148) of a native sequence PRO9871 cDNA, where designated herein as "DNA141423".

Figure 2149 shows the amino acid sequence (SEQ ID NO : 2149) derived from the coding sequence in Figure 2148.

Figure 2150 shows a nucleotide sequence (SEQ ID NO : 2150) of a native sequence PRO19597 cDNA, where designated herein as "DNA143292".

Figure 2151 shows the amino acid sequence (SEQ ID NO : 2151) derived from the coding sequence in Figure 2150.

Figure 2152 shows a nucleotide sequence (SEQ ID NO : 2152) of a native sequence PRO19600 cDNA, where designated herein as "DNA149876".

Figure 2153 shows the amino acid sequence (SEQ ID NO : 2153) derived from the coding sequence in Figure 2152.

Figure 2154 shows a nucleotide sequence (SEQ ID NO : 2154) of a native sequence PRO28700 cDNA, where designated herein as "DNA176108".

Figure 2155 shows the amino acid sequence (SEQ ID NO : 2155) derived from the coding sequence in Figure 2154.

Figure 2156 shows a nucleotide sequence (SEQ ID NO : 2156) of a native sequence PRO617 cDNA, where designated herein as "DNA48309".

Figure 2157 shows the amino acid sequence (SEQ ID NO : 2157) derived from the coding sequence in Figure 2156.

Figure 2158 shows a nucleotide sequence (SEQ ID NO : 2158) of a native sequence PRO844 cDNA, where designated herein as "DNA328248".

Figure 2159 shows the amino acid sequence (SEQ ID NO : 2159) derived from the coding sequence in Figure 2158.

Figure 2160 shows a nucleotide sequence (SEQ ID NO : 2160) of a native sequence PR071057 cDN 2160 is a clone designated herein as "DNA304488".

Figure 2161 shows the amino acid sequence (SEQ ID NO : 2161) derived from the coding sequence in Figure 2160.

Figure 2162 shows a nucleotide sequence (SEQ ID NO : 2162) of a native sequence PRO1160 cDN/ is a clone designated herein as "DNA328249".

Figure 2163 shows the amino acid sequence (SEQ ID NO : 2163) derived from the coding sequence in Figure 2162.

Figure 2164 shows a nucleotide sequence (SEQ ID NO : 2164) of a native sequence PRO1246 cDN/ 2164 is a clone designated herein as "DNA64885".

Figure 2165 shows the amino acid sequence (SEQ ID NO : 2165) derived from the coding sequence in Figure 2164.

Figure 2166 shows a nucleotide sequence (SEQ ID NO : 2166) of a native sequence PRO82061 cDN 2166 is a clone designated herein as "DNA328250".

Figure 2167 shows the amino acid sequence (SEQ ID NO : 2167) derived from the coding sequence in Figure 2166.

Figure 2168 shows a nucleotide sequence (SEQ ID NO : 2168) of a native sequence PR084147 cDN 2168 is a clone designated herein as "DNA328251".

Figure 2169 shows the amino acid sequence (SEQ ID NO : 2169) derived from the coding sequence ( in Figure 2168.

Figure 2170 shows a nucleotide sequence (SEQ ID NO : 2170) of a native sequence PR037534 cDN 2170 is a clone designated herein as "DNA227071".

Figure 2171 shows the amino acid sequence (SEQ ID NO : 2171) derived from the coding sequence in Figure 2170.

Figure 2172 shows a nucleotide sequence (SEQ ID NO : 2172) of a native sequence PRO84148 cDN 2172 is a clone designated herein as "DNA328252".

Figure 2173 shows the amino acid sequence (SEQ ID NO : 2173) derived from the coding sequence in Figure 2172.

Figure 2174 shows a nucleotide sequence (SEQ ID NO2174 : ) of a native sequence PR02561 cDNA is a clone designated herein as "DNA833070".

Figure 2175 shows the amino acid sequence (SEQ ID NO : 2175) derived from the coding sequence in Figure 2174.

Figure 2176 shows a nucleotide sequence (SEQ ID NO : 2176) of a native sequence PR037544 cDN 2176 is a clone designated herein as "DNA227081".

Figure 2177 shows the amino acid sequence (SEQ ID NO : 2177) derived from the coding sequence in Figure 2176.

Figure 2178 shows a nucleotide sequence (SEQ ID NO : 2178) of a native sequence PR034252 cDN 2178 is a clone designated herein as "DNA216500".

Figure 2179 shows the amino acid sequence (SEQ ID NO : 2179) derived from the coding sequence in Figure 2178.

Figure 2180 shows a nucleotide sequence (SEQ ID NO : 2180) of a native sequence PR084149 cDN 2180 is a clone designated herein as "DNA328253".

Figure 2181 shows the amino acid sequence (SEQ ID NO : 2181) derived from the coding sequence ( in Figure 2180.

Figure 2182 shows a nucleotide sequence (SEQ ID NO : 2182) of a native sequence PR02763 cDNA is a clone designated herein as "DNA88359".

Figure 2183 shows the amino acid sequence (SEQ ID NO : 2183) derived from the coding sequence in Figure 2182.

Figure 2184 shows a nucleotide sequence (SEQ ID NO : 2184) of a native sequence PRO11581 cDN 2184 is a clone designated herein as "DNA328254".

Figure 2185 shows the amino acid sequence (SEQ ID NO : 2185) derived from the coding sequence in Figure 2184.

Figure 2186 shows a nucleotide sequence (SEQ ID NO : 2186) of a native sequence PR035988 cDN 2186 is a clone designated herein as "DNA225525".

Figure 2187 shows the amino acid sequence (SEQ ID NO : 2187) derived from the coding sequence in Figure 2186.

Figure 2188 shows a nucleotide sequence (SEQ ID NO : 2188) of a native sequence PR034253 cDN 2188 is a clone designated herein as "DNA216501".

Figure 2189 shows the amino acid sequence (SEQ ID NO : 2189) derived from the coding sequence in Figure 2188.



Figure 2190 shows a nucleotide sequence (SEQ ID NO : 2190) of a native sequence PR036305 cDN, 2190 is a clone designated herein as "DNA324774".

Figure 2191 shows the amino acid sequence (SEQ ID NO : 2191) derived from the coding sequence, in Figure 2190.

Figure 2192 shows a nucleotide sequence (SEQ ID NO : 2192) of a native sequence PR036134 cDN, 2192 is a clone designated herein as "DNA225671".

Figure 2193 shows the amino acid sequence (SEQ ID NO : 2193) derived from the coding sequence, in Figure 2192.

Figure 2194 shows a nucleotide sequence (SEQ ID NO : 2194) of a native sequence PR037076 cDN, 2194 is a clone designated herein as "DNA226613".

Figure 2195 shows the amino acid sequence (SEQ ID NO : 2195) derived from the coding sequence, in Figure 2194.

Figure 2196 shows a nucleotide sequence (SEQ ID NO : 2196) of a native sequence PR084150 cDN 2196 is a clone designated herein as "DNA328255".

Figure 2197 shows the amino acid sequence (SEQ ID NO : 2197) derived from the coding sequence, in Figure 2196.

Figure 2198 shows a nucleotide sequence (SEQ ID NO : 2198) of a native sequence PRO12564 cDN 2198 is a clone designated herein as "DNA150971".

Figure 2199 shows the amino acid sequence (SEQ ID NO : 2199) derived from the coding sequence, in Figure 2198.

Figure 2200 shows a nucleotide sequence (SEQ ID NO : 2200) of a native sequence PR02892 cDNA is a clone designated herein as "DNA88666".

Figure 2201 shows the amino acid sequence (SEQ ID NO : 2201) derived from the coding sequence, in Figure 2200.

Figure 2202 shows a nucleotide sequence (SEQ ID NO : 2202) of a native sequence PR02712 cDNA is a clone designated herein as "DNA88240".

Figure 2203 shows the amino acid sequence (SEQ ID NO : 2203) derived from the coding sequence, in Figure 2202.

Figure 2204 shows a nucleotide sequence (SEQ ID NO : 2204) of a native sequence PR02114 cDNA is a clone designated herein as "DNA328256".

Figure 2205 shows the amino acid sequence (SEQ ID NO : 2205) derived from the coding sequence, in Figure 2204.

Figure 2206 shows a nucleotide sequence (SEQ ID NO : 2206) of a native sequence PR04815 cDNA is a clone designated herein as "DNA103488".

Figure 2207 shows the amino acid sequence (SEQ ID NO : 2207) derived from the coding sequence in Figure 2206.

Figure 2208 shows a nucleotide sequence (SEQ ID NO : 2208) of a native sequence PRO11711 cDNA 2208 is a clone designated herein as "DNA151333".

Figure 2209 shows the amino acid sequence (SEQ ID NO : 2209) derived from the coding sequence in Figure 2208.

Figure 2210 shows a nucleotide sequence (SEQ ID NO : 2210) of a native sequence PR070862 cDNA, 2210 is a clone designated herein as "DNA328257".

Figure 2211 shows the amino acid sequence (SEQ ID NO : 2211) derived from the coding sequence in Figure 2210.

Figure 2212 shows a nucleotide sequence (SEQ ID NO : 2212) of a native sequence PR021960 cDNA, 2212 is a clone designated herein as "DNA192060".

Figure 2213 shows the amino acid sequence (SEQ ID NO : 2213) derived from the coding sequence in Figure 2212.

Figure 2214 shows a nucleotide sequence (SEQ ID NO:) of a native sequence PR084151 cDNA, where clone designated herein as "DNA328258".

Figure 2215 shows the amino acid sequence (SEQ ID NO : 2215) derived from the coding sequence in Figure 2214.

Figure 2216 shows a nucleotide sequence (SEQ ID NO : 2216) of a native sequence PR02620 cDNA is a clone designated herein as "DNA328259".

Figure 2217A-B shows a nucleotide sequence (SEQ ID NO : 2217) of a native sequence PR062620 cDNA 2217 is a clone designated herein as "DNA83176".

Figure 2218 shows the amino acid sequence (SEQ ID NO : 2218) derived from the coding sequence in Figure 2217A-B.

Figure 2219 shows a nucleotide sequence (SEQ ID NO : 2219) of a native sequence PR037793 cDNA, 2219 is a clone designated herein as "DNA227330".

Figure 2220 shows the amino acid sequence (SEQ ID NO : 2220) derived from the coding sequence in Figure 2219.

Figure 2221 shows a nucleotide sequence (SEQ ID NO : 2221) of a native sequence PR084152 cDN, 2221 is a clone designated herein as "DNA328260".

Figure 2222 shows the amino acid sequence (SEQ ID NO : 2222) derived from the coding sequence, in Figure 2221.

Figure 2223 shows a nucleotide sequence (SEQ ID NO : 2223) of a native sequence PR037676 cDN, 2223 is a clone designated herein as "DNA227213".

Figure 2224 shows the amino acid sequence (SEQ ID NO : 2224) derived from the coding sequence, in Figure 2223.

Figure 2225 shows a nucleotide sequence (SEQ ID NO : 2225) of a native sequence PR083477 cDN, 2225 is a clone designated herein as "DNA327204".

Figure 2226 shows the amino acid sequence (SEQ ID NO : 2226) derived from the coding sequence, in Figure 2225.

Figure 2227 shows a nucleotide sequence (SEQ ID NO : 2227) of a native sequence PR037316 cDN, 2227 is a clone designated herein as "DNA226853".

Figure 2228 shows the amino acid sequence (SEQ ID NO : 2228) derived from the coding sequence, in Figure 2227.

Figure 2229 shows a nucleotide sequence (SEQ ID NO : 2229) of a native sequence cDNA, wherein : designated herein as "DNA328261".

Figure 2230 shows a nucleotide sequence (SEQ ID NO : 2230) of a native sequence PR020129 cDN, clone designated herein as "DNA171401".

Figure 2231 shows the amino acid sequence (SEQ ID NO : 2231) derived from the coding sequence, in Figure 2230.

Figure 2232 shows a nucleotide sequence (SEQ ID NO : 2232) of a native sequence PR084153 cDN, 2232 is a clone designated herein as "DNA328262".

Figure 2233 shows the amino acid sequence (SEQ ID NO : 2233) derived from the coding sequence, in Figure 2232.

Figure 2234 shows a nucleotide sequence (SEQ ID NO : 2234) of a native sequence PR04645 cDNA is a clone designated herein as "DNA328263".

Figure 2235 shows the amino acid sequence (SEQ ID NO : 2235) derived from the coding sequence, in Figure 2234.

Figure 2236A-B shows a nucleotide sequence (SEQ ID NO : 2236) of a native sequence PR037137 c 2236 is a clone designated herein as "DNA226674".

Figure 2237 shows the amino acid sequence (SEQ ID NO : 2237) derived from the coding sequence in Figure 2236A-B.

Figure 2238 shows a nucleotide sequence (SEQ ID NO : 2238) of a native sequence PR036538 cDN 2238 is a clone designated herein as "DNA226075".

Figure 2239 shows the amino acid sequence (SEQ ID NO : 2239) derived from the coding sequence in Figure 2238.

Figure 2240 shows a nucleotide sequence (SEQ ID NO : 2240) of a native sequence PRO12087 cDN 2240 is a clone designated herein as "DNA328264".

Figure 2241 shows the amino acid sequence (SEQ ID NO : 2241) derived from the coding sequence in Figure 2240.

Figure 2242 shows a nucleotide sequence (SEQ ID NO : 2242) of a native sequence PR04805 cDNA is a clone designated herein as "DNA103478".

Figure 2243 shows the amino acid sequence (SEQ ID NO : 2243) derived from the coding sequence in Figure 2242.

Figure 2244 shows a nucleotide sequence (SEQ ID NO : 2244) of a native sequence PRO1192 cDNA 2244 is a clone designated herein as "DNA328265".

Figure 2245 shows the amino acid sequence (SEQ ID NO : 2245) derived from the coding sequence in Figure 2244.

Figure 2246 shows a nucleotide sequence (SEQ ID NO : 2246) of a native sequence PRO12125 cDN 2246 is a clone designated herein as "DNA328266".

Figure 2247 shows the amino acid sequence (SEQ ID NO : 2247) derived from the coding sequence in Figure 2246.

Figure 2248A-B shows a nucleotide sequence (SEQ ID NO : 2248) of a native sequence PRO12864 2248 is a clone designated herein as "DNA328267".

Figure 2249 shows the amino acid sequence (SEQ ID NO : 2249) derived from the coding sequence in Figure 2248A-B.

Figure 2250A-B shows a nucleotide sequence (SEQ ID NO : 2250) of a native sequence PR021704 c 2250 is a clone designated herein as "DNA188192".

Figure 2251 shows the amino acid sequence (SEQ ID NO : 2251) derived from the coding sequence in Figure 2250A-B.

Figure 2252 shows a nucleotide sequence (SEQ ID NO : 2252) of a native sequence PRO84154 2252 is a clone designated herein as "DNA328268".

Figure 2253 shows the amino acid sequence (SEQ ID NO : 2253) derived from the coding sequence in Figure 2252.

Figure 2254 shows a nucleotide sequence (SEQ ID NO : 2254) of a native sequence PR02115 cl is a clone designated herein as "DNA328269".

Figure 2255 shows the amino acid sequence (SEQ ID NO : 2255) derived from the coding sequence in Figure 2254.

Figure 2256 shows a nucleotide sequence (SEQ ID NO : 2256) of a native sequence PR04583 cl is a clone designated herein as "DNA103253".

Figure 2257 shows the amino acid sequence (SEQ ID NO : 2257) derived from the coding sequence in Figure 2256.

Figure 2258 shows a nucleotide sequence (SEQ ID NO : 2258) of a native sequence PR0118 cl is a clone designated herein as "DNA52749".

Figure 2259 shows the amino acid sequence (SEQ ID NO : 2259) derived from the coding sequence in Figure 2258.

Figure 2260 shows a nucleotide sequence (SEQ ID NO : 2260) of a native sequence PR069926 , 2260 is a clone designated herein as "DNA287951".

Figure 2261 shows the amino acid sequence (SEQ ID NO : 2261) derived from the coding sequence in Figure 2260.

Figure 2262 shows a nucleotide sequence (SEQ ID NO : 2262) of a native sequence PR038180 , 2262 is a clone designated herein as "DNA227717".

Figure 2263 shows the amino acid sequence (SEQ ID NO : 2263) derived from the coding sequence in Figure 2262.

Figure 2264 shows a nucleotide sequence (SEQ ID NO : 2264) of a native sequence PR09901 cl is a clone designated herein as "DNA328270".

Figure 2265 shows the amino acid sequence (SEQ ID NO : 2265) derived from the coding sequence in Figure 2264.

Figure 2266 shows a nucleotide sequence (SEQ ID NO : 2266) of a native sequence PRO81868 2266 is a clone designated herein as "DNA328271".

Figure 2267 shows the amino acid sequence (SEQ ID NO : 2267) derived from the coding sequence in Figure 2266.

Figure 2268 shows a nucleotide sequence (SEQ ID NO : 2268) of a native sequence PR036024 cDN, 2268 is a clone designated herein as "DNA225561".

Figure 2269 shows the amino acid sequence (SEQ ID NO : 2269) derived from the coding sequence, in Figure 2268.

Figure 2270 shows a nucleotide sequence (SEQ ID NO : 2270) of a native sequence PR070976 cDN, 2270 is a clone designated herein as "DNA328272".

Figure 2271 shows the amino acid sequence (SEQ ID NO : 2271) derived from the coding sequence, in Figure 2270.

Figure 2272 shows a nucleotide sequence (SEQ ID NO : 2272) of a native sequence PR023248 cDN, 2272 is a clone designated herein as "DNA325110".

Figure 2273 shows the amino acid sequence (SEQ ID NO : 2273) derived from the coding sequence, in Figure 2272.

Figure 2274 shows a nucleotide sequence (SEQ ID NO : 2274) of a native sequence PR084155 cDN, 2274 is a clone designated herein as "DNA328273".

Figure 2275 shows the amino acid sequence (SEQ ID NO : 2275) derived from the coding sequence, in Figure 2274.

Figure 2276 shows a nucleotide sequence (SEQ ID NO : 2276) of a native sequence PR033683 cDN, 2276 is a clone designated herein as "DNA210138".

Figure 2277 shows the amino acid sequence (SEQ ID NO : 2277) derived from the coding sequence, in Figure 2276.

Figure 2278A-B shows a nucleotide sequence (SEQ ID NO : 2278) of a native sequence PR037368 c, 2278 is a clone designated herein as "DNA226905".

Figure 2279 shows the amino acid sequence (SEQ ID NO : 2279) derived from the coding sequence, in Figure 2278A-B.

Figure 2280 shows a nucleotide sequence (SEQ ID NO : 2280) of a native sequence PRO12912 cDN, 2280 is a clone designated herein as "DNA328274".

Figure 2281 shows the amino acid sequence (SEQ ID NO : 2281) derived from the coding sequence, in Figure 2280.

Figure 2282 shows a nucleotide sequence (SEQ ID NO : 2282) of a native sequence PRO12752 cDN, 2282 is a clone designated herein as "DNA151907".

Figure 2283 shows the amino acid sequence (SEQ ID NO : 2283) derived from the coding sequence in Figure 2282.

Figure 2284 shows a nucleotide sequence (SEQ ID NO : 2284) of a native sequence PR021687 cDN 2284 is a clone designated herein as "DNA188181".

Figure 2285 shows the amino acid sequence (SEQ ID NO : 2285) derived from the coding sequence in Figure 2284.

Figure 2286 shows a nucleotide sequence (SEQ ID NO : 2286) of a native sequence PR0200 cDNA, is a clone designated herein as "DNA327202".

Figure 2287 shows the amino acid sequence (SEQ ID NO : 2287) derived from the coding sequence in Figure 2286.

Figure 2288 shows a nucleotide sequence (SEQ ID NO : 2288) of a native sequence PR036003 cDN 2288 is a clone designated herein as "DNA225540".

Figure 2289 shows the amino acid sequence (SEQ ID NO : 2289) derived from the coding sequence in Figure 2288.

Figure 2290 shows a nucleotide sequence (SEQ ID NO : 2290) of a native sequence PR084156 cDN 2290 is a clone designated herein as "DNA328275".

Figure 2291 shows the amino acid sequence (SEQ ID NO : 2291) derived from the coding sequence in Figure 2290.

Figure 2292 shows a nucleotide sequence (SEQ ID NO : 2292) of a native sequence PR084157 cDN 2292 is a clone designated herein as "DNA328276".

Figure 2293 shows the amino acid sequence (SEQ ID NO : 2293) derived from the coding sequence in Figure 2292.

Figure 2294 shows a nucleotide sequence (SEQ ID NO : 2294) of a native sequence PR036079 cDN 2294 is a clone designated herein as "DNA328277".

Figure 2295 shows the amino acid sequence (SEQ ID NO : 2295) derived from the coding sequence in Figure 2294.

Figure 2296A-B shows a nucleotide sequence (SEQ ID NO : 2296) of a native sequence PRO12450 2296 is a clone designated herein as "DNA328278".

Figure 2297 shows the amino acid sequence (SEQ ID NO : 2297) derived from the coding sequence in Figure. 2296A-B Figure 2298 shows a nucleotide sequence (SEQ ID NO : 2298) of a native sequel wherein SEQ ID NO : 2298 is a clone designated herein as "DNA327199".

Figure 2299 shows the amino acid sequence (SEQ ID NO : 2299) derived from the coding sequence

in Figure 2298.

Figure 2300 shows a nucleotide sequence (SEQ ID NO : 2300) of a native sequence cDNA, where designated herein as "DNA328279".

Figure 2301 shows a nucleotide sequence (SEQ ID NO : 2301) of a native sequence PRO1213 cDNA 2301 is a clone designated herein as "DNA66487".

Figure 2302 shows the amino acid sequence (SEQ ID NO : 2302) derived from the coding sequence in Figure 2301.

Figure 2303 shows a nucleotide sequence (SEQ ID NO : 2303) of a native sequence PRO82992 cDNA 2303 is a clone designated herein as "DNA326639".

Figure 2304 shows the amino acid sequence (SEQ ID NO : 2304) derived from the coding sequence in Figure 2303.

Figure 2305A-B shows a nucleotide sequence (SEQ ID NO : 2305) of a native sequence PR03849; 2305 is a clone designated herein as "DNA228029".

Figure 2306 shows the amino acid sequence (SEQ ID NO : 2306) derived from the coding sequence in Figure 2305A-B.

Figure 2307 shows a nucleotide sequence (SEQ ID NO : 2307) of a native sequence cDNA, where designated herein as "DNA150981".

Figure 2308 shows a nucleotide sequence (SEQ ID NO : 2308) of a native sequence cDNA, where designated herein as "DNA154390".

Figure 2309A-B shows a nucleotide sequence (SEQ ID NO : 2309) of a native sequence PR08415; 2309 is a clone designated herein as "DNA328280".

Figure 2310 shows the amino acid sequence (SEQ ID NO : 2310) derived from the coding sequence in Figure 2309A-B.

Figure 2311 shows a nucleotide sequence (SEQ ID NO : 2311) of a native sequence cDNA, where designated herein as "DNA328281".

Figure 2312 shows a nucleotide sequence (SEQ ID NO : 2312) of a native sequence PRO11738 cDNA 2312 is a clone designated herein as "DNA151360".

Figure 2313 shows the amino acid sequence (SEQ ID NO : 2313) derived from the coding sequence in Figure 2312.

Figure 2314 shows a nucleotide sequence (SEQ ID NO : 2314) of a native sequence PRO11820 cDNA 2314 is a clone designated herein as "DNA151466".



Figure 2315 shows the amino acid sequence (SEQ ID NO : 2315) derived from the coding sequence in Figure 2314.

Figure 2316 shows a nucleotide sequence (SEQ ID NO : 2316) of a native sequence PRO11863 cl 2316 is a clone designated herein as "DNA151518".

Figure 2317 shows the amino acid sequence (SEQ ID NO : 2317) derived from the coding sequence in Figure 2316.

Figure 2318A-B shows a nucleotide sequence (SEQ ID NO : 2318) of a native sequence PRO8415-2318 is a clone designated herein as "DNA328282".

Figure 2319 shows the amino acid sequence (SEQ ID NO : 2319) derived from the coding sequence in Figure 2319A-B.

Figure 2320 shows a nucleotide sequence (SEQ ID NO : 2320) of a native sequence PRO11899 cl 2320 is a clone designated herein as "DNA151578".

Figure 2321 shows the amino acid sequence (SEQ ID NO : 2321) derived from the coding sequence in Figure 2320.

Figure 2322A-B shows a nucleotide sequence (SEQ ID NO : 2322) of a native sequence cDNA, which clone designated herein as "DNA328283".

Figure 2323A-B shows a nucleotide sequence (SEQ ID NO : 2323) of a native sequence PRO8416-2323 is a clone designated herein as "DNA328284".

Figure 2324 shows the amino acid sequence (SEQ ID NO : 2324) derived from the coding sequence in Figure 2323A-B.

Figure 2325 shows a nucleotide sequence (SEQ ID NO : 2325) of a native sequence PRO12039 cl 2325 is a clone designated herein as "DNA151761".

Figure 2326 shows the amino acid sequence (SEQ ID NO : 2326) derived from the coding sequence in Figure 2325.

Figure 2327 shows a nucleotide sequence (SEQ ID NO : 2327) of a native sequence PRO12052 cl 2327 is a clone designated herein as "DNA151774".

Figure 2328 shows the amino acid sequence (SEQ ID NO : 2328) derived from the coding sequence in Figure 2327.

Figure 2329 shows a nucleotide sequence (SEQ ID NO : 2329) of a native sequence PRO84161 cl 2329 is a clone designated herein as "DNA328285".

Figure 2330 shows the amino acid sequence (SEQ ID NO : 2330) derived from the coding sequence

in Figure 2329.

Figure 2331A-B shows a nucleotide sequence (SEQ ID NO : 2331) of a native sequence PR069594 2331 is a clone designated herein as "DNA287330".

Figure 2332 shows the amino acid sequence (SEQ ID NO : 2332) derived from the coding sequence in Figure 2331A-B.

Figure 2333 shows a nucleotide sequence (SEQ ID NO : 2333) of a native sequence PRO84162 cDNA 2333 is a clone designated herein as "DNA328286".

Figure 2334 shows the amino acid sequence (SEQ ID NO : 2334) derived from the coding sequence in Figure 2333.

Figure 2335 shows a nucleotide sequence (SEQ ID NO : 2335) of a native sequence PR023605 cDNA 2335 is a clone designated herein as "DNA194213".

Figure 2336 shows the amino acid sequence (SEQ ID NO : 2336) derived from the coding sequence in Figure 2335.

Figure 2337 shows a nucleotide sequence (SEQ ID NO : 2337) of a native sequence PR023896 cDNA 2337 is a clone designated herein as "DNA194541".

Figure 2338 shows the amino acid sequence (SEQ ID NO : 2338) derived from the coding sequence in Figure 2337.

Figure 2339A-B shows a nucleotide sequence (SEQ ID NO : 2339) of a native sequence PR024103 cDNA 2339 is a clone designated herein as "DNA194840".

Figure 2340 shows the amino acid sequence (SEQ ID NO : 2340) derived from the coding sequence in Figure 2339A-B.

Figure 2341A-C shows a nucleotide sequence (SEQ ID NO : 2341) of a native sequence PR084163 2341 is a clone designated herein as "DNA328287".

Figure 2342 shows the amino acid sequence (SEQ ID NO : 2342) derived from the coding sequence in Figure 2341A-C.

Figure 2343 shows a nucleotide sequence (SEQ ID NO : 2343) of a native sequence PR069876 cDNA 2343 is a clone designated herein as "DNA328288".

Figure 2344 shows the amino acid sequence (SEQ ID NO : 2344) derived from the coding sequence in Figure 2343.

Figure 2345 shows a nucleotide sequence (SEQ ID NO : 2345) of a native sequence cDNA, wherein designated herein as "DNA196275".

Figure 2346 shows a nucleotide sequence (SEQ ID NO : 2346) of a native sequence PR028564 cDN, 2346 is a clone designated herein as "DNA199066".

Figure 2347 shows the amino acid sequence (SEQ ID NO : 2347) derived from the coding sequence in Figure 2346.

Figure 2348 shows a nucleotide sequence (SEQ ID NO : 2348) of a native sequence cDNA, wherein is designated herein as "DNA328289".

Figure 2349 shows a nucleotide sequence (SEQ ID NO : 2349) of a native sequence PR033767 cDN, 2349 is a clone designated herein as "DNA210233".

Figure 2350 shows the amino acid sequence (SEQ ID NO : 2350) derived from the coding sequence in Figure 2349.

Figure 2351 shows a nucleotide sequence (SEQ ID NO : 2351) of a native sequence PR084164 cDN, 2351 is a clone designated herein as "DNA328290".

Figure 2352 shows the amino acid sequence (SEQ ID NO : 2352) derived from the coding sequence in Figure 2351.

Figure 2353A-B shows a nucleotide sequence (SEQ ID NO : 2353) of a native sequence PRO19724, 2353 is a clone designated herein as "DNA73873".

Figure 2354 shows the amino acid sequence (SEQ ID NO : 2354) derived from the coding sequence in Figure 2353A-B.

Figure 2355A-C shows a nucleotide sequence (SEQ ID NO : 2355) of a native sequence PRO84165, 2355 is a clone designated herein as "DNA328291".

Figure 2356 shows the amino acid sequence (SEQ ID NO : 2356) derived from the coding sequence in Figure 2355A-C.

Figure 2357 shows a nucleotide sequence (SEQ ID NO : 2357) of a native sequence PR084166 cDN, 2357 is a clone designated herein as "DNA328292".

Figure 2358 shows the amino acid sequence (SEQ ID NO : 2358) derived from the coding sequence in Figure 2357.

Figure 2359 shows a nucleotide sequence (SEQ ID NO : 2359) of a native sequence PR063135 cDN, 2359 is a clone designated herein as "DNA328293".

Figure 2360 shows the amino acid sequence (SEQ ID NO : 2360) derived from the coding sequence in Figure 2359.

Figure 2361 shows a nucleotide sequence (SEQ ID NO : 2361) of a native sequence PR058823 cDN,

2361 is a clone designated herein as "DNA270444".

Figure 2362 shows the amino acid sequence (SEQ ID NO : 2362) derived from the coding sequence in Figure 2361.

Figure 2363 shows a nucleotide sequence (SEQ ID NO : 2363) of a native sequence PR051466 cDN 2363 is a clone designated herein as "DNA256405".

Figure 2364 shows the amino acid sequence (SEQ ID NO : 2364) derived from the coding sequence in Figure 2363.

Figure 2365 shows a nucleotide sequence (SEQ ID NO : 2365) of a native sequence PR051081 cDN 2365 is a clone designated herein as "DNA256033".

Figure 2366 shows the amino acid sequence (SEQ ID NO : 2366) derived from the coding sequence in Figure 2365.

Figure 2367 shows a nucleotide sequence (SEQ ID NO : 2367) of a native sequence PR049244 cDN 2367 is a clone designated herein as "DNA254129".

Figure 2368 shows the amino acid sequence (SEQ ID NO : 2368) derived from the coding sequence in Figure 2367.

Figure 2369 shows a nucleotide sequence (SEQ ID NO : 2369) of a native sequence PRO84167 cDN 2369 is a clone designated herein as "DNA328294".

Figure 2370 shows the amino acid sequence (SEQ ID NO : 2370) derived from the coding sequence in Figure 2369.

Figure 2371 shows a nucleotide sequence (SEQ ID NO : 2371) of a native sequence PR049824 cDN 2371 is a clone designated herein as "DNA254725".

Figure 2372 shows the amino acid sequence (SEQ ID NO : 2372) derived from the coding sequence in Figure 2371.

Figure 2373 shows a nucleotide sequence (SEQ ID NO : 2373) of a native sequence PRO84168 cDN 2373 is a clone designated herein as "DNA328295".

Figure 2374 shows the amino acid sequence (SEQ ID NO : 2374) derived from the coding sequence in Figure 2373.

Figure 2375 shows a nucleotide sequence (SEQ ID NO : 2375) of a native sequence PR051817 cDN 2375 is a clone designated herein as "DNA328296".

Figure 2376 shows the amino acid sequence (SEQ ID NO : 2376) derived from the coding sequence in Figure 2375.

Figure 2377 shows a nucleotide sequence (SEQ ID NO : 2377) of a native sequence PR059418 cDN, 2377 is a clone designated herein as "DNA328297".

Figure 2378 shows the amino acid sequence (SEQ ID NO : 2378) derived from the coding sequence c in Figure 2377.

Figure 2379 shows a nucleotide sequence (SEQ ID NO : 2379) of a native sequence PR084169 cDN 2379 is a clone designated herein as "DNA328298".

Figure 2380 shows the amino acid sequence (SEQ ID NO : 2380) derived from the coding sequence c in Figure 2379.

Figure 2381 shows a nucleotide sequence (SEQ ID NO : 2381) of a native sequence PRO132 cDNA, is a clone designated herein as "DNA53532".

Figure 2382 shows the amino acid sequence (SEQ ID NO : 2382) derived from the coding sequence c in Figure 2381.

Figure 2383 shows a nucleotide sequence (SEQ ID NO : 2383) of a native sequence PR051331 cDN, 2383 is a clone designated herein as "DNA256287".

Figure 2384 shows the amino acid sequence (SEQ ID NO : 2384) derived from the coding sequence c in Figure 2383.

Figure 2385 shows a nucleotide sequence (SEQ ID NO : 2385) of a native sequence PR050371 cDN, 2385 is a clone designated herein as "DNA255298".

Figure 2386 shows the amino acid sequence (SEQ ID NO : 2386) derived from the coding sequence c in Figure 2385.

Figure 2387 shows a nucleotide sequence (SEQ ID NO : 2387) of a native sequence PR084170 cDN, 2387 is a clone designated herein as "DNA328299".

Figure 2388 shows the amino acid sequence (SEQ ID NO : 2388) derived from the coding sequence c in Figure 2387.

Figure 2389 shows a nucleotide sequence (SEQ ID NO : 2389) of a native sequence PR084171 cDN, 2389 is a clone designated herein as "DNA328300".

Figure 2390 shows the amino acid sequence (SEQ ID NO : 2390) derived from the coding sequence c in Figure 2389.

Figure 2391 shows a nucleotide sequence (SEQ ID NO : 2391) of a native sequence PR070371 cDN, 2391 is a clone designated herein as "DNA328301".

Figure 2392 shows the amino acid sequence (SEQ ID NO : 2392) derived from the coding sequence c

in Figure 2391.

Figure 2393 shows a nucleotide sequence (SEQ ID NO : 2393) of a native sequence PR058796 cDNA, 2393 is a clone designated herein as "DNA270415".

Figure 2394 shows the amino acid sequence (SEQ ID NO : 2394) derived from the coding sequence, in Figure 2393.

Figure 2395 shows a nucleotide sequence (SEQ ID NO : 2395) of a native sequence PR084172 cDNA, 2395 is a clone designated herein as "DNA328302".

Figure 2396 shows the amino acid sequence (SEQ ID NO : 2396) derived from the coding sequence, in Figure 2395.

Figure 2397 shows a nucleotide sequence (SEQ ID NO : 2397) of a native sequence PR069467 cDNA, 2397 is a clone designated herein as "DNA287178".

Figure 2398 shows the amino acid sequence (SEQ ID NO : 2398) derived from the coding sequence, in Figure 2397.

Figure 2399 shows a nucleotide sequence (SEQ ID NO : 2399) of a native sequence PR084173 cDNA, 2399 is a clone designated herein as "DNA328303".

Figure 2400 shows the amino acid sequence (SEQ ID NO : 2400) derived from the coding sequence, in Figure 2399.

Figure 2401 shows a nucleotide sequence (SEQ ID NO : 2401) of a native sequence PR081319 cDNA, 2401 is a clone designated herein as "DNA324684".

Figure 2402 shows the amino acid sequence (SEQ ID NO : 2402) derived from the coding sequence, in Figure 2401.

Figure 2403 shows a nucleotide sequence (SEQ ID NO : 2403) of a native sequence PR084174 cDNA, 2403 is a clone designated herein as "DNA328304".

Figure 2404 shows the amino acid sequence (SEQ ID NO : 2404) derived from the coding sequence, in Figure 2403.

Figure 2405A-B shows a nucleotide sequence (SEQ ID NO : 2405) of a native sequence cDNA, where clone designated herein as "DNA256131".

Figure 2406 shows a nucleotide sequence (SEQ ID NO : 2406) of a native sequence PR090 cDNA, where clone designated herein as "DNA328305".

Figure 2407 shows the amino acid sequence (SEQ ID NO : 2407) derived from the coding sequence, in Figure 2406.

Figure 2408 shows a nucleotide sequence (SEQ ID NO : 2408) of a native sequence PR084175 cDN,  
2408 is a clone designated herein as "DNA328306".

Figure 2409 shows the amino acid sequence (SEQ ID NO : 2409) derived from the coding sequence  
in Figure 2408.

Figure 2410A-B shows a nucleotide sequence (SEQ ID NO : 2410) of a native sequence cDNA, where  
clone designated herein as "DNA255654".

Figure 2411 shows a nucleotide sequence (SEQ ID NO : 2411) of a native sequence PR084176 cDN,  
2411 is a clone designated herein as "DNA328307".

Figure 2412 shows the amino acid sequence (SEQ ID NO : 2412) derived from the coding sequence  
in Figure 2411.

Figure 2413 shows a nucleotide sequence (SEQ ID NO : 2413) of a native sequence cDNA, wherein :  
designated herein as "DNA254447".

Figure 2414 shows a nucleotide sequence (SEQ ID NO : 2414) of a native sequence PR084177 cDN,  
2414 is a clone designated herein as "DNA328308".

Figure 2415 shows the amino acid sequence (SEQ ID NO : 2415) derived from the coding sequence  
in Figure.

Figure 2416 shows a nucleotide sequence (SEQ ID NO : 2416) of a native sequence cDNA, wherein :  
designated herein as "DNA256422".

Figure 2417 shows a nucleotide sequence (SEQ ID NO : 2417) of a native sequence cDNA, wherein :  
designated herein as "DNA255754".

Figure 2418 shows a nucleotide sequence (SEQ ID NO : 2418) of a native sequence PR050081 cDN,  
2418 is a clone designated herein as "DNA328309".

Figure 2419 shows the amino acid sequence (SEQ ID NO : 2419) derived from the coding sequence  
in Figure 2418.

Figure 2420 shows a nucleotide sequence (SEQ ID NO : 2420) of a native sequence cDNA, wherein :  
designated herein as "DNA254286".

Figure 2421 shows a nucleotide sequence (SEQ ID NO : 2421) of a native sequence cDNA, wherein :  
designated herein as "DNA328310".

Figure 2422 shows a nucleotide sequence (SEQ ID NO : 2422) of a native sequence PR084179 cDN,  
2422 is a clone designated herein as "DNA328311".

Figure 2423 shows the amino acid sequence (SEQ ID NO : 2423) derived from the coding sequence

in Figure 2422.

Figure 2424 shows a nucleotide sequence (SEQ ID NO : 2424) of a native sequence PR082369 cDN, 2424 is a clone designated herein as "DNA325915".

Figure 2425 shows the amino acid sequence (SEQ ID NO : 2425) derived from the coding sequence, in Figure 2424.

Figure 2426A-B shows a nucleotide sequence (SEQ ID NO : 2426) of a native sequence PR058642 c 2426 is a clone designated herein as "DNA270254".

Figure 2427 shows the amino acid sequence (SEQ ID NO : 2427) derived from the coding sequence, in Figure 2426A-B.

Figure 2428 shows a nucleotide sequence (SEQ ID NO : 2428) of a native sequence PR063223 cDN, 2428 is a clone designated herein as "DNA275594".

Figure 2429 shows the amino acid sequence (SEQ ID NO : 2429) derived from the coding sequence, in Figure 2428.

Figure 2430 shows a nucleotide sequence (SEQ ID NO : 2430) of a native sequence PR050363 cDN, 2430 is a clone designated herein as "DNA255289".

Figure 2431 shows the amino acid sequence (SEQ ID NO : 2431) derived from the coding sequence, in Figure 2430.

Figure 2432A-B shows a nucleotide sequence (SEQ ID NO : 2432) of a native sequence PRO84180, 2432 is a clone designated herein as "DNA328312".

Figure 2433 shows the amino acid sequence (SEQ ID NO : 2433) derived from the coding sequence, in Figure 2432.

Figure 2434 shows a nucleotide sequence (SEQ ID NO : 2434) of a native sequence PRO82174 cDN 2434 is a clone designated herein as "DNA325685".

Figure 2435 shows the amino acid sequence (SEQ ID NO : 2435) derived from the coding sequence, in Figure 2434.

Figure 2436 shows a nucleotide sequence (SEQ ID NO : 2436) of a native sequence PR050218 cDN, 2436 is a clone designated herein as "DNA255137".

Figure 2437 shows the amino acid sequence (SEQ ID NO : 2437) derived from the coding sequence, in Figure 2436.

Figure 2438 shows a nucleotide sequence (SEQ ID NO : 2438) of a native sequence PRO84181 cDN, 2438 is a clone designated herein as "DNA328313".



Figure 2439 shows the amino acid sequence (SEQ ID NO : 2439) derived from the coding sequence in Figure 2438.

Figure 2440 shows a nucleotide sequence (SEQ ID NO : 2440) of a native sequence PR084182 cDNA 2440 is a clone designated herein as "DNA328314".

Figure 2441 shows the amino acid sequence (SEQ ID NO : 2441) derived from the coding sequence in Figure 2440.

Figure 2442 shows a nucleotide sequence (SEQ ID NO : 2442) of a native sequence PR084183 cDNA 2442 is a clone designated herein as "DNA328315".

Figure 2443 shows the amino acid sequence (SEQ ID NO : 2443) derived from the coding sequence in Figure 2442.

Figure 2444 shows a nucleotide sequence (SEQ ID NO : 2444) of a native sequence PR050231 cDNA 2444 is a clone designated herein as "DNA255151".

Figure 2445 shows the amino acid sequence (SEQ ID NO : 2445) derived from the coding sequence in Figure 2444.

Figure 2446 shows a nucleotide sequence (SEQ ID NO : 2446) of a native sequence cDNA, where designated herein as "DNA256055".

Figure 2447 shows a nucleotide sequence (SEQ ID NO : 2447) of a native sequence PR084184 cDNA 2447 is a clone designated herein as "DNA328316".

Figure 2448 shows the amino acid sequence (SEQ ID NO : 2448) derived from the coding sequence in Figure 2447.

Figure 2449 shows a nucleotide sequence (SEQ ID NO : 2449) of a native sequence PR069493 cDNA 2449 is a clone designated herein as "DNA328317".

Figure 2450 shows the amino acid sequence (SEQ ID NO : 2450) derived from the coding sequence in Figure 2449.

Figure 2451 shows a nucleotide sequence (SEQ ID NO : 2451) of a native sequence PR084185 cDNA 2451 is a clone designated herein as "DNA328318".

Figure 2452 shows the amino acid sequence (SEQ ID NO : 2452) derived from the coding sequence in Figure 2451.

Figure 2453 shows a nucleotide sequence (SEQ ID NO : 2453) of a native sequence PR038240 cDNA 2453 is a clone designated herein as "DNA227777".

Figure 2454 shows the amino acid sequence (SEQ ID NO : 2454) derived from the coding sequence in Figure 2453.

in Figure 2453.

Figure 2455 shows a nucleotide sequence (SEQ ID NO : 2455) of a native sequence cDNA, wherein designated herein as "DNA328319".

Figure 2456A-B shows a nucleotide sequence (SEQ ID NO : 2456) of a native sequence PRO84187 2456 is a clone designated herein as "DNA328320".

Figure 2457 shows the amino acid sequence (SEQ ID NO : 2457) derived from the coding sequence in Figure.

Figure 2458 shows a nucleotide sequence (SEQ ID NO : 2458) of a native sequence PRO84188 cDNA 2458 is a clone designated herein as "DNA328321".

Figure 2459 shows the amino acid sequence (SEQ ID NO : 2459) derived from the coding sequence in Figure 2458.

Figure 2460 shows a nucleotide sequence (SEQ ID NO : 2460) of a native sequence PRO54445 cDNA 2460 is a clone designated herein as "DNA260519".

Figure 2461 shows the amino acid sequence (SEQ ID NO : 2461) derived from the coding sequence in Figure 2460.

Figure 2462 shows a nucleotide sequence (SEQ ID NO : 2462) of a native sequence cDNA, wherein designated herein as "DNA328322".

Figure 2463 shows a nucleotide sequence (SEQ ID NO : 2463) of a native sequence cDNA, wherein designated herein as "DNA257960".

Figure 2464 shows a nucleotide sequence (SEQ ID NO : 2464) of a native sequence PRO69531 cDNA 2464 is a clone designated herein as "DNA328323".

Figure 2465 shows the amino acid sequence (SEQ ID NO : 2465) derived from the coding sequence in Figure 2464.

Figure 2466 shows a nucleotide sequence (SEQ ID NO : 2466) of a native sequence cDNA, wherein designated herein as "DNA262448".

Figure 2467 shows a nucleotide sequence (SEQ ID NO : 2467) of a native sequence PRO84189 cDNA 2467 is a clone designated herein as "DNA328324".

Figure 2468 shows the amino acid sequence (SEQ ID NO : 2468) derived from the coding sequence in Figure 2467.

Figure 2469 shows a nucleotide sequence (SEQ ID NO : 2469) of a native sequence cDNA, wherein designated herein as "DNA259231".

Figure 2470 shows a nucleotide sequence (SEQ ID NO : 2470) of a native sequence cDNA, wherein designated herein as "DNA259493".

Figure 2471A-B shows a nucleotide sequence (SEQ ID NO : 2471) of a native sequence PRO84190 2471 is a clone designated herein as "DNA328325".

Figure 2472 shows the amino acid sequence (SEQ ID NO : 2472) derived from the coding sequence in Figure 2471.

Figure 2473 shows a nucleotide sequence (SEQ ID NO : 2473) of a native sequence PRO84191 cDNA 2473 is a clone designated herein as "DNA328326".

Figure 2474 shows the amino acid sequence (SEQ ID NO : 2474) derived from the coding sequence in Figure 2473.

Figure 2475 shows a nucleotide sequence (SEQ ID NO : 2475) of a native sequence cDNA, wherein designated herein as "DNA260507".

Figure 2476 shows a nucleotide sequence (SEQ ID NO : 2476) of a native sequence cDNA, wherein designated herein as "DNA262598".

Figure 2477 shows a nucleotide sequence (SEQ ID NO : 2477) of a native sequence cDNA, wherein designated herein as "DNA259663".

Figure 2478 shows a nucleotide sequence (SEQ ID NO : 2478) of a native sequence cDNA, wherein designated herein as "DNA260543".

Figure 2479 shows a nucleotide sequence (SEQ ID NO : 2479) of a native sequence cDNA, wherein designated herein as "DNA262755".

Figure 2480 shows a nucleotide sequence (SEQ ID NO : 2480) of a native sequence cDNA, wherein designated herein as "DNA262761".

Figure 2481 shows a nucleotide sequence (SEQ ID NO : 2481) of a native sequence PRO84192 cDNA 2481 is a clone designated herein as "DNA328327".

Figure 2482 shows the amino acid sequence (SEQ ID NO : 2482) derived from the coding sequence in Figure 2481.

Figure 2483 shows a nucleotide sequence (SEQ ID NO : 2483) of a native sequence PRO84193 cDNA 2483 is a clone designated herein as "DNA328328".

Figure 2484 shows the amino acid sequence (SEQ ID NO : 2484) derived from the coding sequence in Figure 2483.

the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequence. The percentage of amino acid residues in a candidate sequence that are identical with the PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the best possible sequence identity, and not considering any conservative substitutions as part of the identity, is determined. Determining percent amino acid sequence identity can be achieved in various ways that are known in the art, using publicly available computer software such as BLAST, BLAST-2, ALIGN or MegAlign. The art can determine appropriate parameters for measuring alignment, including any adjustments to the alignment over the full length of the sequences being compared. For purposes herein, the values are generated using the sequence comparison computer program ALIGN-2, version 1.9. The ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison program is a registered trademark of Genentech, Inc. and the source code shown in Table 1 below has been filed with the U.S. Patent and Trademark Office, Washington D. C. 20559, where it is registered under U. S. Patent No. 6,038,507.

Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available to researchers in the field of protein structure prediction. The program is available from the source code provided in Table 1 to the authors of this manuscript.

The ALIGN-2 program should be compiled for use on a UNIX operating system, prefer comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the amino acid sequence A to, with, or against a given amino acid sequence B (which contains amino acid sequence A that has or comprises a certain % amino acid sequence identity to, or against, amino acid sequence B) is calculated as follows: 100 times the fraction  $X/Y$  where X is the number of amino acid residues in A that align with amino acid residues in B, and Y is the number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. Examples of % amino acid sequence identity calculations using this method, Tables 1-3, are provided below. The amino acid sequence identity of the amino acid sequence designated "Comparison P" to the amino acid sequence designated "PRO", wherein "PRO" represents the amino acid sequence of a hypothetical protein, is calculated as follows:

and "X", "Y" and "Z" each represent different hypothetical amino acid residues.

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained immediately preceding paragraph using the ALIGN-2 computer program.

However, % amino acid sequence identity values may also be obtained as described below by using the program (Altschul et al., Methods in Enzymology 266: 460-480 (1996)). Most of the WU-BLAST-2 sequence identity values are set to default values, i.e., the adjustable parameters, are set with the following values: span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. When the % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native amino acid sequence of the PRO polypeptide against which the PRO polypeptide is compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence B is the amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of interest.

Percent amino acid sequence identity may also be determined using the sequence comparison program of Altschul et al., Nucleic Acids Res. 25: 3389-3402 (1997). The NCBI-BLAST2 sequence comparison program is available at <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, MD. Several search parameters, wherein all of those search parameters are set to default values including: yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value cutoff = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be a nucleic acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows: 100 times the fraction X/Y where X is the number of amino acid sequence matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and Y is the number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

"PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, as disclosed herein or any other fragment of a full-length PRO polypeptide herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 82% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 84% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 86% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 88% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 90% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 92% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 94% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 96% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 98% nucleic acid sequence identity to a full-length native sequence PRO polypeptide, alternatively at least about 99% nucleic acid sequence identity to a full-length native sequence PRO polypeptide.

sequence as discussed herein, a full-length PRO polypeptide sequence, with or without the signal sequence, as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein, a fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass a full-length PRO polypeptide sequence as disclosed herein.

Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 600 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences is the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum alignment. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in a number of ways, for instance, using publicly available computer software such as BLAST, BLAST-2, BLAST-N, and the like. For purposes herein, however, % nucleic acid sequence identity values are generated using a computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in the source code of the computer program ALIGN-2, which is publicly available from Genentech, Inc. and the source code of the computer program ALIGN-2 has been filed with user documentation in the U. S. Copyright Office, Washington D. C. , 20559, with the title "ALIGN-2: A Program for Aligning Nucleic Acid Sequences".

Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., 460 Point San Bruno Blvd., South San Francisco, California 94080.

The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital VAX/VMS. The ALIGN-2 program parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be a nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows: 100 times the fraction W/Z where W is the number of nucleotides in C that match the sequence alignment program ALIGN-2 in that program's alignment of C and D, and Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. Examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "Reference DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic acid sequence of interest. "PRO-DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are of the PRO polypeptide sequence as disclosed herein, immediately preceding paragraph using the ALIGN-2 computer program.

However, % nucleic acid sequence identity values may also be obtained as described below by using a program (Altschul et al., Methods in Enzymology 266: 460-480 (1996)). Most of the WU-BLAST-2 parameters are set to default values, i.e., the adjustable parameters, are set with the following values: span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. The % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest having a

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Pero  
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Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed; participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it facilitates translation. Generally, "operably linked" means that the DNA sequences being linked are connected by a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adapts in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyclonal anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal" refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the population comprising the population are identical except for possible naturally occurring mutations that may be present.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and is a function of calculation dependent upon probe length, washing temperature, and salt concentration. In general, for temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization of denatured DNA to reanneal when complementary strands are present in an environment below the higher the degree of desired homology between the probe and hybridizable sequence, the higher the stringency can be used. As a result, it follows that higher relative temperatures would tend to make the reaction more stringent while lower temperatures less so. For additional details and explanation of stringency of hybridization, see, e.g., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated in 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C).

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization temperature, ionic strength and % SDS less stringent than those described above. An example of moderate stringency is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize hybridization stringency, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO polypeptide and a tag polypeptide. The tag polypeptide has enough residues to provide an epitope against which an antibody can be raised such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides include at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, 10-20).



As used herein, the term "immunoadhesin" designates an heterologous protein (an "adhesin") with the effector function of immunoadhesins comprising a fusion of an amino acid sequence and binding site of an antibody (i.e., is "heterologous" because the immunoadhesin molecule typically is a fusion of an antibody amino acid sequence with a receptor or a ligand). The immunoglobulin constant domain of the immunoglobulin molecule typically is replaced by a receptor or a ligand. Examples of immunoglobulin constant domains that can be replaced by a receptor or a ligand include IgG-1, IgG-2, IgG-3, or IgG-4 constant domains.

"Active" or "activity" for the purposes herein refers to form (a) immunological activity of native or naturally-occurring PR inhibitory or stimulatory) caused by a native or naturally-occurring antibody against an antigenic epitope possessed by a native or naturally-occurring antibody to induce the production of an antibody against the antigenic epitope.

The term "antagonist" is used in the broadest sense, and includes a biological activity of a native PRO polypeptide disclosed herein, and includes any molecule that mimics a biological or antagonist molecules specifically include agonist or antagonist sequence variants of native PRO polypeptides, peptides, identifying agonists or antagonists of a PRO polypeptide antagonist molecule and measuring a detectable change in the polypeptide.

"Treatment" refers to both therapeutic treatment and progression down (lessen) the targeted pathologic condition or disorder as well as those prone to have the disorder or the

"Chronic" administration refers to administration of the agent to maintain the initial therapeutic effect (activity) for an extended period of time.

"Intermittent" administration is treatment that is not consecutive.

"Mammal" for purposes of treatment refers to any animal (other than a human) and zoo, sports, or pet animals, such as dogs, cats, cattle and horses.

Administration" in combination with "one or more further th administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers known to those skilled in the art, such as aqueous or non-aqueous solutions, emulsions, suspensions, and the like. Examples of physiological saline solutions are isotonic sodium chloride solution, Ringer's solution, and lactated Ringer's solution. Examples of other organic acids; antioxidants including ascorbic acid; such as serum albumin, gelatin, or immunoglobulins; hydrous alcohols; glycerine; glycols; amino acids; glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, mannose, or dextrins; chelating agents such as EDTA; sequestering agents; buffers; stabilizers; surfactants; preservatives; and/or nonionic surfactants such as TWEEN, SLES, and the like.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of an antibody. Examples of antibody fragments include Fab, Fab', F (ab')<sub>2</sub>, and Fv fragments; diabodies; linear antibody; single-chain antibody molecules; and multispecific antibodies. (See, e.g., Protein Eng. 8 (10): 1057-1062 [1995]).

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each having one antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin digestion of an antibody produces antigen-binding fragments and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site, i.e., it contains one heavy-chain variable domain in tight, non-covalent association with one light-chain variable domain. It is in this CDR of each variable domain that an antigen-binding site is located on the surface of the VH-VL complex. CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain of the heavy chain. Fab fragments differ from Fv fragments by the addition of a few residues at the carboxy terminus of light chain constant domain and one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for residue (s) of the constant domains bear a free thiol group. F (ab')<sub>2</sub> antibody fragments originally were Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are known in the art.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two classes, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins are divided into five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and each of these is further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

"Single-chain Fv" or "scFv" antibody fragments comprise the VH and VL domains of antibody, wherein the variable domains of both heavy and light chains are connected by a polypeptide linker between the C-terminus of the heavy chain and the N-terminus of the light chain, which enables the scFv to form the desired structure for antigen binding. For a review of scFv, see Plüsch et al., *Monoclonal Antibodies*, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-284.

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragment variable domain (VH) connected to a light-chain variable domain (VL) in the same polypeptide chain (that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with domains of another chain and create two antigen-binding sites). Diabodies are described, for example, in EP 404,097; WO 93/11161; and Hollinger et al., *Proc. Natl. Acad. Sci. USA*, 90: 6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a complex mixture of other antibodies, e.g., from a mixture of antibodies secreted by a population of hybridoma cells. Contaminant components of its natural environment are materials which would interfere with the use of the antibody, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous materials. The antibody will be purified (1) to greater than 95% by weight of antibody as determined by SDS-PAGE, (2) to a degree sufficient to obtain at least 15% yield of antibody, and (3) to homogeneity by SDS-PAGE. The antibody may be purified by a variety of methods, including but not limited to, ion exchange chromatography, size exclusion chromatography, immunoaffinity chromatography, and other methods. The isolated antibody may be further purified by a variety of methods, including but not limited to, ion exchange chromatography, size exclusion chromatography, immunoaffinity chromatography, and other methods. The isolated antibody may be further purified by a variety of methods, including but not limited to, ion exchange chromatography, size exclusion chromatography, immunoaffinity chromatography, and other methods.

An antibody that "specifically binds to" or is "specific for" a particular polypeptide or an epitope on a polypeptide binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to other polypeptides or epitopes on other polypeptides.

The word "label" when used herein refers to a detectable compound or composition which is conjugated to an antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotopes) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound to a detectable product.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can be attached. The solid phase may be a solid support, such as glass, plastic, paper, or metal, or a solid matrix, such as agarose, polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity column). This term also includes a discontinuous solid phase of discrete particles such as those described in U.S. Pat. No. 4,150,007.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome form a bilayer formation, similar to the lipid arrangement of biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

The term "immune related disease" means a disease in which a component of the immune system or otherwise contributes to a morbidity in the mammal. Also included are diseases in which stimulation of the immune response has an ameliorative effect on progression of the disease. Included within this term are inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunoneoplasia, etc.

The term "T cell mediated disease" means a disease in which T cells directly or indirectly mediate or contribute to the pathogenesis of the disease in a mammal. The T cell mediated disease may be associated with cell mediated effects, humoral effects, or even effects associated with B cells if the B cells are stimulated, for example, by the lymphocyte stimulating agent.

As used herein the term "psoriasis" is defined as a condition characterized by the eruption of circumferential, silvery-scaled macropapules preeminently on the elbows, knees, scalp or trunk.

The term "effective amount" is a concentration or amount of a PRO polypeptide and/or agonist/antagonist achieving a particular stated purpose. An "effective amount" of a PRO polypeptide or agonist or antagonist is determined empirically. Furthermore, a "therapeutically effective amount" is a concentration or amount of a PRO polypeptide or agonist/antagonist which is effective for achieving a stated therapeutic effect. This amount may also

The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells, or causes the destruction of cells. The term is intended to include radioactive isotopes (e.g., I131, I125, Y90 and R223), chemotherapeutic agents, and toxins such as enzymatically active toxins of bacterial, fungal, plant or animal origin, or

A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of



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V W X Y /* A */ {2, 0, 2, 0, 0, 4, 1, -1, 1, 0, 1, 2, 1, 0, _M, 1, 0, -2, 1, 1, 0, 0, 6, 0, 3, 0}, /* B */ {0,
2, _M, -1, 1, 0, 0, 0, -2, -5, 0, -3, 1}, /* C */ {-2, -4, 15, -5, -5, -4, -3, -2, 0, -5, -6, -5, -4, _M, -3, -5, -4, 0, -2,
4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, _M, -1, 2, -1, 0, 0, -2, -7, 0, -4, 2}, /* E */ {0, 2, -5, 3, 4, -5, 0, 1, -2, 0, 0, -3,
0, -4, 3}, /* F */ {-4, -5, -4, -6, -5, 9, -5, -2, 1, 0, -5, 2, 0, -4, _M, -5, -4, -3, -3, 0, -1, 0, 0, 7, -51, /* G */ {1, 0,
0, _M, 1, 1, 3, 1, 0, 0, 1, -7, 0, -5, 0}, /* H */ {-1, 1, -3, 1, 1, -2, -2, -6, -2, 0, 2, 2, 2, _M, 0, 3, 2, 1, 1,
2, -2, 1, -3, -2, 5, 0, -2, 2, -2, _M, -2, -2, -1, 0, 4, -5, 0, -1, -2}, /* J */ {0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,
0, 0}, /* K */ {1, 0, -5, 0, 0, -5, -2, 0, -2, 0, 5, -3, 0, 1, _M, -1, 1, 3, 0, 0, -2, -3, 0, -4, 0}, /* L */ {-2, 3, -6, -4,
3, -2, -3, -3, -1, 0, -2, 0, -1, -2, /* M */ {-1, -2, -5, -3, -2, 0, 0, 4, 6, -2, _M, -2, -1, 0, -2, -1, 0, 2, -4, 0,
2, 2, 0, 1, 3, 2, 2, _M, -1, 1, 0, 1, 0, -2, -4, 0, -2, 1}, /* O */ {M, M, M, M, M, M, M, M, M, M, M, M, M, M, M, M, M,
M, M, M}, /* P */ {1, 1, 3, 1, 1, 5, 1, 0, -2, 0, 1, 3, 2, -1, M, 6, 0, 0, 1, 0, 0, -1, -6, 0, -5, 0}, /* Q */ {0,
1, 1, M, 0, 4, 1, -1, 1, 0, -2, -5, 0, 4, 3}, /* R */ {-2, 0, -4, -1, -4, -3, -2, -2, 0, -3, 0, 0, _M, 0, 1, 6, 0, -1,
0, 0, -3, 1, 1, 0, 0, 3, 2, 1, _M, 1, 1, 0, 2, 1, 0, -1, -2, 0, -3, 0}, /* T */ {1, 0, -2, 0, -3, -1, 0, 0, 0,
5, 0, -3, 0}, /* U */ {0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0}, /* V */ {0, -2,
_M, -1, -2, -2, -1, 0, 0, 4, -6, 0, -2, -2, /* W */ {-6, -5, -8, -7, 0, -7, -3, -5, 0, -3, -2, -4, -4, _M, -6, -5, 2, -2, -5, 0, -6,
0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0}, /* Y */ {-3, -3, 0, -4, 4, 7, -5, 0, -1, 0, -4, -1, -2,
10, -4, /* Z */ {0, 1, -5, 2, 3, -5, 0, 2, -2, 0, 0, -2, -1, 1, -M, 0, 3, 0, 0, 0, -2, -6, 0, -4, 4}}, Table 1 (cont) *
<ctype, h> #define MAXJMP 16 /* max jumps in a diag */ #define MAXGAP 24 /* don't continue to p
#define JMPS 1024 /* max jumps in an path */ #define MX 4 /* save if there's at least MX-1 bases sin
value of matching bases */ #define DMIS 0 /* penalty for mismatched bases */ #define DINSO 8 /* p
DINS1 1 /* penalty per base */ #define PINSO 8 /* penalty for a gap */ #define PINS1 4 /* penalty per
[MAXJMP] /* size of jmp (neg for dely) */ unsigned short x [MAXJMP] /* base no. of jmp in seq x */
struct diag { int score; /* score at last jmp */ long offset; /* offset of prev block */ short jmp; /* current
list of jmps */ }; struct path { int spc; /* number of leading spaces */ short n [JMPS] /* size of jmp (g
jmp (last elem before gap) */; char *ofile; /* output file name */ char *namex [2] /* seq names : ge
name for err msgs */ char *seqx [2] /* seqs : getseqs () */ int dmax; /* best diag : nw () */ int dmaxC
dna : main () /* int endgaps; /* set if penalizing end gaps */ int gapx, gapy; /* total gaps in seqs */ in
ngapx, ngapy; /* total size of gaps */ int smax; /* max score : nw () */ int *xbm; /* bitmap for matchin
in jmp file */ struct diag *dx; /* holds diagonals */ struct path pp [2]; /* holds path for seqs */ char *ca
*strcpy (); char *getseq (), *g_calloc (); Table 1 (cont) /* Needleman-Wunsch alignment program
where file1 and file2 are two dna or two protein sequences. * The sequences can be in upper-or low
ambiguity Any lines beginning with ' ;' >or< are ignored * Max file length is 65535 (limited by unsig
sequence with 1/3 or more of its elements ACGTU is assumed to be DNA * Output is in the file "alig
create a tmp file in/tmp to hold info about traceback. * Original version developed under BSD 4. 3 o
#include "day. h" static dbval [26] = {1, 14, 2, 13, 0, 0, 4, 11, 0, 0, 12, 0, 3, 15, 0, 0, 0, 5, 6, 8, 7,
= {1, 21 (1 « ('D'-A (1 « ('N'-A')), 4, 8, 16, 32, 64, 128, 256, 0xPFFFFF, 1 « 10, 1 « 11, 1 « 12, 1
« 17, 1 « 18, 1 « 19, 1 « 20, 1 « 21, 1 « 22, 1 « 23, 1 « 24, 1 « 25 (1 « ('E'-A)) | (1 « ('Q'-A)) 1 < 23
(l < < (Q-A)) main (ac, av) main int ac; char *av []; { prog = av [0]; if (ac != 3) { fprintf (stderr, "usage
fprintf (stderr, "where file1 and file2 are two dna or two protein sequences. In", ); fprintf (stderr, "The s
lower-case\n"); fprintf (stderr, "Any lines beginning with ' ;' or< are ignored\n"); fprintf (stderr, "Output
exit (1); } namex [0] = av [1]; namex [1] = av [2]; seqx [0] = getseq (namex [0], &len0); seqx [1] = ge
(dna) ? dbval : pbval; endgaps = 0; /* 1 to penalize endgaps */ ofile = "align. out"; /* output file il nw
possible jmps */ readjmps (); /* get the actual jmps */ print (); /* print stats, alignment */ cleanup (0)
Table 1 (cont) /* do the alignment, return best score : main () * dna : values in Fitch and Smith, PN
pro : PAM 250 values * When scores are equal, we prefer mismatches to any gap, prefer * a new g
gap, and prefer a gap in seqx * to a gap in seq y. */ nw () nw { char *px, *py; /* seqs and ptrs */ int *
dely */ int ndex, dely; /* keep track of dely */ int *tmp; /* for swapping rowO, rowl */ int mis; /* score
insertion penalties */ register id; /* diagonal index register i; /* jmp index */ register *colO, *coll; /* sc
xx, yy; /* index into seqs */ dx = (struct diag *) g_calloc ("to get diag", lenO+lenl+1, sizeof (struct diag
get ndely", lenl+1, sizeof (int)); dely = (int *) g_calloc ("to get dely", lenl+1, sizeof (int)); colO = (int *)
sizeof (int)); coll = (int *) g_calloc ("to get coll", lenl+1, sizeof (int)); insO = (dna) ? DINSO : PINSO
smax = -10000; if (endgaps) { for (colO [0] = dely [0] = -insO, yy = 1; yy <= lenl; yy++) { colO [yy] =
ndely [w] = vv : colO [0] = 0; /* Waterman Bull Math Biol 84 */ } else for (vv = 1; vv <= lenl; vv++) { d

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matrix */ for (px = seqx [0], xx = 1; xx <= lenO; px++, xx++) { /* initialize first entry in col */ if (
=-(insO+insl); else coll [O] = delx = colO [0]-insl; ndelx = xx; } else { coll [0] = 0; delx =-insO
for (py = seqx [1], yy = 1; yy <= lenl; py++, yy++) { mis = colO [yy-l]; if (dna) mis += (xbrn [*px
else mis += day [*px-A [*py-A]; /* update penalty for del in x seq; * favor new del over ongo
endgaps x/ if (endgaps 11 ndely [yy] < MAXGAP) { if (colO [yy]-insO >= delx [yy]) { delx [yy] =
1; } else { delx [yy] = insl; ndely [yy] ++; } } else { if (colO [yy]- (insO+insl) >= delx [yy]) { delx
[yy] = 1; } else ndely [yy] ++; } /* update penalty for del in y seq; * favor new del over ongon
MAXGAP) { if (coll [yy-l]-insO >= delx) { delx = coll [yy-l]- (insO+insl); ndelx = 1; } else { delx-
[yy-l]- (insO+insl) >= delx) { delx = coll [yy-l]- (insO+insl); ndelx = 1; } else ndelx++; } /* pick 1
mis over any del and delx over delx */ Table 1 (cont) ... nw id=xx-yy+lenl-1; if (mis >= delx &{
else if (delx >= delx [yy]) { coll [yy] = delx; ij = dx [id]. ijmp if (dx [id] jp. n [O] && ( ! dna 11 (nd
[ij] +MX) 11 mis > dx [id]. score+DINSO)) { dx [id]. ijmp++; if (++ij >= MAXJMP) { writeimps (it
offset = offset; offset += sizeof (struct jmp) + sizeof (offset); } dx [id] jp. n [ij] = ndelx; dx [id] j
else { coll [yy] = delx [yy]; ij = dx [id]. ijmp; if (dx [id]. jp. n [O] && ( ! dna (ndely [yy] >= MAXJ
mis > dx [id]. score+DINSO)) { dx [id]. ijmp++; if (++ij >= MAXJMP) { writeimps (id); ij = dx [id
offset += sizeof (struct jmp) + sizeof (offset); } dx [id]. jp. n [ij] =ndely [yy]; dx [id] jp. x [ij] = x
lenO && yy < lenl) { /* last col */ if (endgaps) coll [yy]=insO+insl* (lenl-yy); if (coll [yy] > smax)
(endgaps && xx < lenO) coll [yy-1]= insO+ins 1 * (lenO-xx); if (coll [yy-l] > smax) { smax = co
colO = coll; coll = tmp; } (void) free ( (char *) ndely); (void) free ( (char *) delx); (void) free (
coll); Table 1 (cont) /* ** printO--only routine visible outside this module * static: * getmat (-)
matches: print () * pr_align ()--print alignment of described in array p []: print () * dumpblock (
numbers, stars: pr_align () * umso--put out a number line: dumpblock () * putline ()--put out a
dumpblock () * stars: dumpblockQ * stripname ()--strip any path and pre
h" #define SPC 3 #define PLINE 256/* maximum output line */ #define P_SPC 3/* space betw
day [26] [26]; int olen; /* set output line length */ FILE *fx; /* output file */ print () print (int lx, ly
( (fx = fopen (ofile, "w")) == 0) { fprintf (stderr, "%s: can't write %s\n", prog, ofile); cleanup (l)
(length = %d) \n", namex [O], lenO); fprintf (fx, "<second sequence: %s (length = %d) \n", n
lenO; ly = lenl; firstgap = lastgap = 0; if (dmax < lenl-1) { /* leading gap in x */ pp [0]. spc = fir
spc; } else if (dmax > lenl-1) { /* leading gap in y */ pp [1]. spc = firstgap = dmax- (lenl-1); lx=-
trailing gap in x */ lastgap = lenO-dmaxO-1; lx = lastgap; } else if (dmaxO > lenO-1) { /* trailin
1); ly=- lastgap; } getmat (lx, ly, firstgap, lastgap); pr_align (); Table 1 (cont) /* * trace bac
static getmat (lx, ly, firstgap, lastgap) getmat int lx, ly; /* "core" (minus endgaps) */ int firstgap,
int nm, iO, il, sizO, sizl; char outx [32]; double pct; register nO, nl; register char *pO, *pl; /*
sizO = sizl = 0; pO = seqx [0] + pp [1]. spc; pl = seqx [1] + pp [0]. spc; nO pp [1]. spc + 1; nl =
&& *pl) { if (sizO) { pl++; sizO--; } else if (sizl) { pO++; nO++; sizl--; } else { if (xbrn [*pc
== pp [0]. x [iO]) sizO = pp [0]. n [iO++]; if (nl++ == pp [1]. x [il]) sizl = pp [1]. n [il++]; pO++; pl-
penalizing endgaps, base is the shorter seq * else, knock off overhangs and take shorter core
lenO: lenl; else lx = (lx < ly) ? lx : ly; pct = 100. * (double) nm/(double) lx; fprintf (fx, "\n"); fpi
overlap of %d : %. 2f percent similarity\n", nm, (nm== 1) ? "" : "es", lx, pct); Table 1 (cont) frii
d", gapx) ... getmat if (gapx) { (void) sprintf (outx, " (%d %d %s %s)", ngapx, (dna) ? "base" : "resi
(fx, "%s", outx); fprintf (fx, ", gaps in second sequence: %d", gapx); if (gapx) { (void) sprintf (
(dna) ? "base" : "residue", (ngapy==1) ? "" : "s"); fprintf (fx, "%s", outx); } if (dna) fprintf (fx, "\n<
= %d, gap penalty = %d + %d per base) \n", smax, DMAT, DMS, DINSO, DINS1); else fpi
PAM 250 matrix, gap penalty = %d + %d per residue) \n", smax, PINSO, PINS1); if (endgap
left endgap : %d %s %s, right endgap : %d %s %s \n", firstgap, (dna) ? "base" : "residue", (fir
(dna) ? "base" : "residue", (lastgap == 1) ? "" : "s"); else fprintf (fx, "<endgaps not penalized\n");
checking */ static lmax; /* lengths of stripped file names */ static ij [2]; /* jmp index for a path */
current line */ static ni [2]; /* current elem number--for gapping */ static siz [2]; static char *ps
char *po [2]; /* ptr to next output char slot */ static char out [2] [P_LINE]; /* output line */ static
*/ /* * print alignment of described in struct path pp [] */ static pralign () pralign (int nn; /* char
0, lmax = 0; i < 2; i++) { nn = stripname (namex [i]); if (nn > lmax) lmax = nn; nc [i] = 1; ni [i
[i]; po [i] = out [i]; Table 1 (cont) for (nn = nm = 0, more = 1; more;) { ... pr_align for (i = mo
more of this sequence ? */ if ( ! *ps [i]) continue; more++; if (op [i]. soc) { /* leading space */ t

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[i]) /* in a gap */ *po[i] += "-"; siz[i]--; } else /* we're putting a seq element */ *po[i] =
(*ps[i]); po[i]++; ps[i]++; /* are we at next gap for this seq ? */ if (ni[i] == pp[i].x[i])
this location */ siz[i] = pp[i].n[i][i]++; while (ni[i]++) pp[i].x[i][i]) siz[i] += pp[i].n[i]
&& nn) { dumpblock(); for (i=0; i<2; i++) po[i] = out[i]; nn=0; } } /* * dump a block
pr_alignO */ static dumpblock() { dumpblock i; register i; for (i=0; i<2; i++) *po[i] = 0;
(En', fx); for (i=0; i<2; i++) { if (*out[i] && (*out[i] != " ")) { if (i==0) nums(i);
== O && *out[i]) fprintf(fx, star); if (i-1) nums(i); } } * put out a number line : dumpbloc
in out[] holding seq line *i { char nline[P_LINE]; register i, j; register char *pn, *px, *py;
++, pn++; *pn = "", for (i=nc[ix], py = out[ix]; *py; py++, pn++) { if (*py == "PY" || *py ==
= 1) { j= (i<0) ? -i : i; for (px = pn; j; j/=10, px--) *px = %10 + '0'; if (i < 0) *px--; else *pn
nline; *pn; pn++; (void) puts(*pn, fx); (void) puts(En', fx); } /* * put out a line (name, [n
putline (x) putline int ix; { Table 1 Table 1 (cont') ... putline int i; register char *px; for (p
++, i++) (void) puts(*px, fx); for (i < lmax+P_SPC; i++) (void) puts(" ", fx); /* these col
1) * nc[] is number at start of current line xl for (px = out[ix]; *px; px++) (void) puts(*px
a line of stars (seqs always in out [O], out [I]) : dumpblock() 1 static stars () stars { int i;
[O][I] (*out [O] == "&&" * (po [0]) == "&&") ) { *out [I] (*out [I] == "&&" * (po [I]) == "&&") return; px
+ "="; for (pO = out [O], pl = out [I]; *pO && *pl; pO++, pl++) { if (isalpha (*pO) && isalph
{ cl=" "; nm++; } else if (!dna && day [*pO-A] [*pl-A > 0] cx = , else cx = " ";
1 (cont') /* * strip path or prefix from pn, return len : pr_align () */ static stripname (pn) str
path) /* { register char *px, *py; puy=0; for (px = pn; *px; px++) if (*px == '/') py=px+1; if
(pn); } Table 1 (cont') /* * cleanup ()--cleanup any tmp file * getseq ()--read in seq, set d
with error checkin * readjumpsQ--get the good jumps, from tmp file if necessary * writejumps
file : nw () /* #include "nw. h" #include <sys/file. h> char *jname = "tmp/homgXXXXXX", /*
* cleanup tmp file */ long lseek (); /* * remove any tmp file if we blow * cleanup (i) clean
(i); } /* * read, return ptr to seq, set dna, len, maxlen * skip lines starting with '<', or * seq
(file, len) getseq char *file; /* file name */ int *len; /* seq len */ { char line[1024], *pseq; n
*fp; if ((fp = fopen (file, "r")) == O) { fprintf (stderr, "%s : can't read %s\n", prog, file); exit
1024, fp) { if (*line == " "); if (*line == "<" *Hne == continue; for (px = line; *px != En'; px++)
if ( (pseq = malloc ( (tlen+6))) == O) { fprintf (stderr, "%s : malloc () failed to ge
exit (i); } pseq [O] = pseq [I] = pseq [2] = pseq [3] = '\0'; Table 1 (cont') ... getseq py = ps
(fgets (line, 1024, fp) { if (*line == " "); if (*line == "<" *line == "<" continue; for (px = line; *px
*px; else if (islower (*px)) *py++ = toupper (*px); if (index ("ATGCU", * (py-I)) natgc++;
= natgc > (tlen/3); return (pseq+4); } char * galloc (msg, nx, sz) g alloc char *msg; /* f
number and size of elements */ char *px, *calloc (); if ( (px = calloc ( (unsigned) nx, (uns
(stderr, "%s : galloc () failed %s (n=%d, sz=%d) \n", prog, msg, nx, sz); exit (i); } rel
tmp file, set pp [], reset dmax : main () /* readjumps () readjumps { int fd = -1; int siz, i0, i1;
( (fd = open (jname, O_RDONLY, 0) < 0) { fprintf (stderr, "%s : can't open () %s\n", pro
0, dmaxO = dmax, xx = lenO; i++; } while (1) { for (j = dx [dmax].jmp; j >= 0 && dx [d
readjumps if (j < 0 && dx [dmax].offset && fj) { (void) lseek (fd, dx [dmax].offset, 0); (voic
(struct jmp)); (void) read (fd, (char *) &dx [dmax].offset, sizeof (dx [dmax].offset)); dx [
if (i >= JMPS) { fprintf (stderr, "%s : too many gaps in alignment\n", prog); cleanup (i); }
[dmax].jp. x[i]; dmax += siz; if (siz < 0) /* gap in second seq */ pp [I]. n [i] = -siz; xx +=
xx-dmax + lenl-1; gapy++; ngapy = siz; /* ignore MAXGAP when doing endgaps */ siz =
MAXGAP; i++; } else if (siz > 0) /* gap in first seq */ pp [O]. n [iO] = siz; pp [O]. x [iO] =
MAXGAP when doing endgaps */ siz = (siz < MAXGAP || endgaps) ? siz : MAXGAP; iO+
jumps */ for (j = 0, iO--, j < iO; j++, iO--) { i = pp [O]. n [j]; n [j] = pp [O]. n [iO]; pp
= pp [O]. x [iO]; pp [O]. x [iO] = i; } for (j=O, il--; j < il; j++) { i = pp [I]. n [j]; pp
[i]; pp [I]. x [i] = pp [I]. x [il]; x [il] = i; if (fd >= 0) (void) close (fd); if (fn) { (void) unli
(cont') * * write a filled jmp struct offset of the prev one (if any) : nw () /* writejumps (ix) wri
{ if (mktemp (jname) < 0) { fprintf (stderr, "%s : can't mktemp () %s\n", prog, jname); cle
O) { fprintf (stderr, "%s : can't write %s\n", prog, jname); exit (i); } } (void) fwrite ( (char
(void) fwrite ( (char *) &dx [ix].offset, sizeof (dx [ix].offset), 1, fj); } Table 2 PRO XXXXX
Comparison Protein XXXXXYYYYYYY (Length = 12 amino acids) % amino acid sequen

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synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by restriction enzymes and isolating the desired fragment. Yet another suitable technique involves is fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides of the DNA fragment are employed at the 5' and 3' termini in the PCR. Preferably, PRO polypeptide disclosed here at least one biological and/or immunological activity with the native PRO polypeptide.

In particular embodiments, conservative substitutions of interest are shown in Table 6 under the h substitutions. If such substitutions result in a change in biological activity, then more substantial cl substitutions in Table 6, or as further described below in reference to amino acid classes, are intr screened.

Table 6 Original Exemplary Preferred Residue Substitutions Ala (A) val ; leu ; ile val (N) gln ; his ; lys ; arg gln Asp (D) glu glu Cys (C) ser ser Gln (Q) asn asn Glu (E) asp asp Gly (G) lys ; arg ile (I) leu ; val ; met ; ala ; phe ; norleucine Leu (L) norleucine ; ile ; val ; met ; ala ; phe ile (M) leu ; phe ; ile leu Phe (F) leu ; val ; ile ; ala ; tyr leu Pro (P) ala ala Ser (S) thr thr thr Thr (T) ser thr ; phe ; thr ; ser phe Val (V) ile ; leu ; met ; phe ; ala ; norleucine leu Substantial modifications in identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Natural divided into groups based on common side-chain properties: (1) hydrophobic: norleucine, met, ala hydrophilic: cys, ser, thr; (3) acidic: asp, glu; (4) basic: asn, gln, his, lys, arg; (5) residues that influence and (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another, residues also may be introduced into the conservative substitution sites or, more preferably, into the sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (si) alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., *Nucl. Acids R.*, al., *Nucl. Acids Res.*, 10: 6487 (1987)], cassette mutagenesis [Wells et al., *Gene*, 34: 315 (1985), mutagenesis [Wells et al., *Philos. Trans. R. Soc.*

London SerA, 317: 415 (1986) ] or other known techniques can be performed on the cloned DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a the preferred scanning amino acids are relatively small, neutral amino acids.

Such amino acids include alanine, glycine, -serine, and cysteine. Alanine is typically a preferred  $\alpha$  group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the  $\pi$  variant [Cunningham and Wells, *Science*, 244: 1081-1085 (1989)].

Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently exposed positions [Creighton, *The Proteins*, (W. H. Freeman & Co., N. Y.): Chothia, J.



modification includes reacting targeted amino acid residues of a PRO polypeptide with an o capable of reacting with selected side chains or the N-or C-terminal residues of the PRO. D useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for PRO antibodies, and vice-versa.

Commonly used crosslinking agents include, e. g., 1, 1-bis (diazocetyl) -2-phenylethane, g esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including dithiobis (succinimidy] propionate), bifunctional maleimides such as bis-N-maleimido-1, 8-azidophenyl) dithio] propionimide.

Other modifications include deamidation of glutamyl and asparagyl residues to the corresponding residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups, methylation of the  $\alpha$ -amino groups of lysine, arginine, and histidine side chains [T. E. Creighton, Molecular Properties, W. H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the PRO polypeptide included within the scope of the present invention is the native glycosylation pattern. "Altering the native glycosylation pattern" is in the context of deleting one or more carbohydrate moieties found in native sequence PRO (either by removing or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more carbohydrate moieties to the native sequence PRO. In addition, the phrase includes qualitative changes in glycosylation, involving a change in the nature and proportions of the various carbohydrate moieties.

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the native glycosylation pattern, for example, by the addition of, or substitution by, one or more serine or threonine residues (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases which will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is the addition of glycosylation sites to the polypeptide. Such methods are described in the art, e. g., in WO 87/05 and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished by mutational substitution of codons encoding for amino acid residues that serve as targets for deglycosylation techniques are known in the art and described, e. g., in <BR> <BR> for instance, Biochem. Biophys., 259: 52 (1987) and by Edge et al., Anal.

Biochem., 118: 131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides consisting of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138 : 350

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one or more polymers, e. g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the context of, e. g., 4,496, 689; 4,301, 144; 4,670, 417; 4,791, 192 or 4, 179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising a heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide.

Sequences identified in such library screening methods can be compared and aligned to other known sequences available in public databases such as GenBank or other private sequence databases. Sequence identity (or nucleotide level) within defined regions of the molecule or across the full-length sequence can be known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates that have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells Host cells are transfected or transformed with expression vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. Methods and protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Molecular Cloning: A Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan. For example, CaCl<sub>2</sub>, CaPO<sub>4</sub>, liposome-mediated and electroporation. Depending on the host cell used, transformation standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* for transformation of certain plant cells, as described by Shaw et al., Gene, 23: 315 (1983) and WO 89/01989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of G. Virology, 52: 456-457 (1978) can be employed. General aspects of mammalian cell host system transformations are described in U. S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to Solingen et al., J. Bact., 130: 946 (1977) and Hsiao et al., Proc. Natl. Acad. Sci. (USA), 76: 3829 (1979). Methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial transformation, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transformation, see Keown et al., Methods in Enzymology, 185: 527-537 (1990) and Mansour et al., Nature, 336: 342 (1989).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, and eukaryote. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,501); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,501). Suitable eukaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Salmonella*, e.g., *Sabnoizella typhimurium*, *Serratia*, e.g., *Serratia narcescaras*, and *Sizigella*, as well as *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is a host or parent host because it is a common host strain for recombinant DNA product fermentations and secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to express genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 complete genotype total; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* (ATCC 55,244), which has the complete genotype *toril ptr3 phoA E15 (argF-lac) 169 degP ompT kai* 37D6, which has the complete genotype *tonna ptr3 plaoA E15 (argF-lac) 169 degP onapT rbs7 avlG* 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain periplasmic protease disclosed in U. S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, in addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeasts are suitable cloning hosts.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeasts are suitable cloning hosts.

Both expression and cloning vectors contain a nucleic acid sequence that is recognized by restriction enzymes. Such sequences are well known for a variety of bacterial

pbk3322 is suitable for most Gram-negative bacteria, the  $\lambda$  plasmid origin is suitable for yeast, and polyoma, adenovirus, VSV or BPV are useful for cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker, that encode proteins that (a) confer resistance to antibiotics or other toxins, e. g., ampicillin, neomycin, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e. g., D-alanine racemase for *Bacillus*.

An example of suitable selectable markers for mammalian cells are those that enable the identification of cells that have taken up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell which is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Acad. Sci. USA, 77: 4216 (1980).

A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinct (1979); Kingsman et al., *Gene*, 7: 141 (1979); Tschemper et al., *Gene*, 10: 157 (1980)].

The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in the absence of tryptophan. Jones, Genetics, 85: 12 (1977).

Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nu mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoti prokaryotic hosts include the  $\beta$ -lactamase and lactose promoter systems [Chang et al., Nature, 275 Nature, 281: 544 (1979)], alkaline phosphatase, a tryptophan (trp) promoter system [Goeddel, Nuc (1980); EP 36,776], and hybrid promoters such as the tac promoter [deBoer et al. Proc. Natl. Acad.

Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S. D. ) sequence operator PRO:

Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3- $\alpha$ -phosphoglycerate kinase [Hitzeman et al., J. Biol. Chem., 255: 2073 (1980)] or other glycolytic enzymes [Enzyme Reg., 7: 149 (1968); Holland, Biochemistry, 17: 4900 (1978)], such as enolase, glyceraldehyde hydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase

Other yeast promoters, which are inducible promoters having the additional advantage of transcriptional regulation, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, and phosphoglycerate kinase. These promoters are associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and galactose utilization. Suitable vectors and promoters for use in yeast expression are found in Table 1.

PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters of viruses such as polyoma virus, fowlpox virus (UK 2,211, 504 published 5 July 1989), adenovirus (s papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Vi heterologous mammalian promoters, e. g., the actin promoter or an immunoglobulin promoter, and provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an  $\epsilon$  vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a p transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include

late side of the replication origin (bp 100-2/U), the cytomegalovirus early promoter side of the replication origin, and adenovirus enhancers. The enhancer may be split PRO coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal multicellular organisms) will also contain sequences necessary for the termination. Such sequences are commonly available from the 5' and, occasionally 3', untranslated cDNAs. These regions contain nucleotide segments transcribed as polyadenylated mRNA encoding PRO.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis are described in Gething et al., *Nature*, 293: 620-625 (1981); Mantei et al., *Nature*, 117, 058.

4. Detecting Gene Amplification/Expression Gene amplification and/or expression is, for example, by conventional Southern blotting, Northern blotting to quantitate the trans-

*Natl. Acad. Sci. USA*, 77: 5201-5205 (1980) ], dot blotting (DNA analysis), or *in situ* probe, based on the sequences provided herein. Alternatively, antibodies may be used including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-p labeled and the assay may be carried out where the duplex is bound to a surface, for example, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of the PRO. Immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal.

Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a DNA sequence provided herein or against exogenous sequence fused to a PRO polypeptide.

5. Purification of Polypeptide Forms of PRO may be recovered from culture media. If the PRO is bound, it can be released from the membrane using a suitable detergent solution (e.g., SDS). Cells employed in expression of PRO can be disrupted by various physical or chemical methods, such as sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following are suitable purification procedures: by fractionation on an ion-exchange column; ethyl acetate extraction; chromatography on silica or on a cation-exchange resin such as DEAE; chromatography on Sepharose; gel filtration using, for example, Sephadex G-75; protein A Sepharose; and metal chelating columns to bind epitope-tagged forms of the PRO. Various other methods are known in the art and described for example in DeWitt et al., *Protein Purification: Principles and Practice*, Springer-Verlag, New York (1981). The location of the PRO in the cell, the nature of the production process used and the particular host cell may also be considered.

E. Tissue Distribution The location of tissues expressing the PRO can be identified by immunohistochemical staining. The location of such genes provides information about which tissues express the PRO. The location of such genes provides information about which tissues stimulate and inhibit activities of the PRO polypeptides. The location of a gene

As noted before, gene expression in various tissues may be measured by conventional Southern blotting to quantitate the transcription of mRNA (Thomas, Proc. Natl. Acad. Sci. USA, 77: 5201-5205 [1980]). Direct in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein, may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and/or DNA-protein duplexes.

Gene expression in various tissues, alternatively, may be measured by immunological methods, such as staining of tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of a gene. Useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal antibodies prepared in any mammal.

Conveniently, the antibodies may be prepared against a native sequence of a PRO polypeptide or against a DNA sequence encoding the PRO polypeptide or against an exogenous sequence fused to the PRO polypeptide and encoding a specific antibody epitope. General techniques for generating antibodies for Northern blotting and in situ hybridization are provided below.

**F. Antibody Binding Studies** The activity of the PRO polypeptides can be further verified by antibody binding studies. The ability of anti-PRO antibodies to inhibit the effect of the PRO polypeptides, respectively, on tissue cells, antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies, the results are described herein below.

Antibody binding studies may be carried out in any known assay method, such as competitive binding assays, sandwich assays, and immunoprecipitation assays. Zola, Monoclonal Antibodies: A Manual of Techniques, 2nd ed., Academic Press, Inc., 1987).

Competitive binding assays rely on the ability of a labeled standard to compete with the test sample for a limited amount of antibody. The amount of target protein in the test sample is inversely proportional to the amount of antibody bound. To facilitate determining the amount of standard that becomes bound, the standard and the test sample are incubated before or after the competition, so that the standard and analyte that are bound to the antibody are conveniently separated from the standard and analyte which remain unbound.

Sandwich assays involve the use of two antibodies, each capable of binding to a different immunogen on a protein to be detected. In a sandwich assay, the test sample analyte is bound by a first antibody which is immobilized on a solid support, and thereafter a second antibody binds to the analyte, thus forming an insoluble three-part complex. No. 4,376, 110. The second antibody may itself be labeled with a detectable moiety (direct sandwich assay) or an anti-immunoglobulin antibody that is labeled with a detectable moiety (indirect sandwich assay). In a sandwich assay, in which case the detectable moiety is an enzyme.

For immunohistochemistry, the tissue sample may be fresh or frozen or may be embedded in paraffin or other preservative such as formalin, for example.

**G. Cell-Based Assays** Cell-based assays and animal models for immune related diseases such as psoriasis, further understand the relationship between the genes and polypeptides identified herein and the development of psoriasis.

In a different approach, cells of a cell type known to be involved in psoriasis are transfected with the cDNA of these cDNAs to stimulate or inhibit psoriasis is analyzed.

Suitable cells can be transfected with the desired gene, and monitored for such functional activity. Then be used to test the ability of poly-or monoclonal antibodies or antibody compositions to inhibit transfected with the coding sequences of the genes identified herein can further be used to identify treatment of psoriasis.

In addition, primary cultures derived from transgenic animals (as described below) can be used in although stable cell lines are preferred. Techniques to derive continuous cell lines from transgenic art (see, e. g. , Small et al., *Mol. Cell. Biol.* 5: 642-648 [1985]).

H. Animal Models The results of cell based in vitro assays can be further verified using in vivo animal psoriasis. A variety of well known animal models can be used to further understand the role of the development and pathogenesis of psoriasis, and to test the efficacy of candidate therapeutic agent other antagonists of the native polypeptides, including small molecule antagonists. The in vivo natural predictive of responses in human patients. Animal models of immune related diseases include both recombinant (transgenic) animals. Non-recombinant animal models include, for example, rodent, e models can be generated by introducing cells into syngeneic mice using standard techniques, e. g. vein injection, spleen implantation, intraperitoneal implantation, implantation under the renal capsule

Graft-versus-host disease occurs when immunocompetent cells are transplanted into immunosuppressed donor cells recognize and respond to host antigens. The response can vary from life threatening cases of diarrhea and weight loss.

Graft-versus-host disease models provide a means of assessing T cell reactivity against MHC antigens. A suitable procedure is described in detail in Current Protocols in Immunology, above, under

An animal model for skin allograft rejection is a means of testing the ability of T cells to mediate in measure of their role in transplant rejection. The most common and accepted models use murine experiments have shown that skin allograft rejection is mediated by T cells, helper T cells and killer antibodies. Auchincloss, H. Jr. and Sachs, D. H., *Fundamental Immunology*, 2nd ed. , W. E. Paul et al. 1989, 889-992. A suitable procedure is described in detail in Current Protocols in Immunology, above, rejection models which can be used to test the compounds of the invention are the allogeneic heart by Tanabe, M. et al, *Transplantation* (1994) 58: 23 and Tinubu, S. A. et al, *J.*

*Immunol.* (1994) 4330-4338.

Contact hypersensitivity is a simple delayed type hypersensitivity in vivo assay of cell mediated immune procedure, cutaneous exposure to exogenous haptens which gives rise to a delayed type hypersensitivity measured and quantitated. Contact sensitivity involves an initial sensitizing phase followed by an effector phase occurs when the T lymphocytes encounter an antigen to which they have had previous contact occur, making this an excellent model of human allergic contact dermatitis. A suitable procedure is *Protocols in Immunology*, Eds. J. E. Cologan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach and Sons, Inc. , 1994, unit 4.2. See also Grabbe, S. and Schwarz, T, *Immun.*

*Today* 19 (1) : 37-44 (1998).

Additionally, the compounds of the invention can be tested on animal models for psoriasis like disease cell pathogenesis for psoriasis. The compounds of the invention can be tested in the scid/scid mouse M. P. et al, *Nat. Med.* (1997) 3: 183, in which the mice demonstrate histopathologic skin lesions resulting

Recombinant (transgenic) animal models can be engineered by introducing the coding the genome of animals of interest, using standard techniques for producing transgenic for transgenic manipulation include, without limitation, mice, rats, rabbits, guinea pigs, primates, e. g., baboons, chimpanzees and monkeys. Techniques known in the art to include pronuclear microinjection (Hoppe and Wanger, U. S. Patent No. 4,873, 191); re lines (e. g., Van der Putten et al., Proc. Natl. Acad. Sci. USA 82,6148-615 [1985]); ger (Thompson et al., Cell 56, 313-321 [1989]); electroporation of embryos (Lo, Mol. Cell. mediated gene transfer (Lavitrano et al., Cell 57,717-73 [1989]). For review, see, for e

For the purpose of the present invention, transgenic animals include those that carry th ("mosaic animals"). The transgene can be integrated either as a single transgene, or ir to-tail tandems. Selective introduction of a transgene into a particular cell type is also f technique of Lasko et al., Proc. Natl.

Acad. Sci. USA 89,6232-636 (1992).

The expression of the transgene in transgenic animals can be monitored by standard t

For example, Southern blot analysis or PCR amplification can be used to verify the intr mRNA expression can then be analyzed using techniques such as in situ hybridization immunocytochemistry.

The animals may be further examined for signs of immune disease pathology, for exar determine infiltration of immune cells into specific tissues. Blocking experiments can al animals are treated with the compounds of the invention to determine the extent of the of the compounds. In these experiments, blocking antibodies which bind to the PRO p are administered to the animal and the effect on immune function is determined.

Alternatively, "knock out" animals can be constructed which have a defective or altered herein, as a result of homologous recombination between the endogenous gene encoc DNA encoding the same polypeptide introduced into an embryonic cell of the animal. F polypeptide can be used to clone genomic DNA encoding that polypeptide in accordan the genomic DNA encoding a particular polypeptide can be deleted or replaced with ar selectable marker which can be used to monitor integration. Typically, several kilobase 5' and 3' ends) are included in the vector [see e. g., Thomas and Capecchi, Cell, 51: 50: recombination vectors]. The vector is introduced into an embryonic stem cell line (e. g. introduced DNA has homologously recombined with the endogenous DNA are selecte The selected cells are then injected into a blastocyst of an animal (e. g., a mouse or r Bradley, in Teratocarcinomas and Embryonic Stem Cells: A Practical Approach, E. J. 152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female term to create a "knock out" animal. Progeny harboring the homologously recombined I standard techniques and used to breed animals in which all cells of the animal contain Knockout animals can be characterized for instance, for their ability to defend against development of pathological conditions due to absence of the polypeptide.

I. ImmunoAdjuvant Therapy In one embodiment, the immunostimulating compounds oi immunoAdjuvant therapy for the treatment of tumors (cancer). It is now well establishe



specific antigens. One group of tumor antigens, encoded by the MAGE, BAGE and GAGE families, normal tissues, but are expressed in significant amounts in tumors, such as melanomas, lung tumor bladder carcinomas. DeSmet, C. et al., (1996) *Proc. Natl. Acad. Sci. USA*, 93: 7149. It has been shown that cells induces tumor regression and an antitumor response both in vitro and in vivo. Melero, I. et al., 1992; Kwon, E. D. et al., *Proc. Natl. Acad. Sci. USA* (1997) 94: 8099; Lynch, D. H. et al., *Nature Med* and Lotze, M. T., *J. Immunol.* (1998) 21: 114. The stimulatory compounds of the invention can be administered alone or together with a growth regulating agent, cytotoxic agent or chemotherapeutic agent, to stimulate activation and an antitumor response to tumor antigens. The growth regulating, cytotoxic, or chemotherapeutic agent administered in conventional amounts using known administration regimens. Immunostimulating agent invention allows reduced amounts of the growth regulating, cytotoxic, or chemotherapeutic agents to be administered to the patient.

J. Screening Assays for Drug Candidates Screening assays for drug candidates are designed to identify or complex with the polypeptides encoded by the genes identified herein or a biologically active fragment thereof. Such screening assays interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays are amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds, including soluble peptides, (poly) peptide-immunoglobulin fusions, and, in particular, antibodies including, without limitation, monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and versions of such antibodies or fragments, as well as human antibodies and antibody fragments. The variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, which are well characterized in the art.

All assays are common in that they call for contacting the drug candidate with a polypeptide encoded by the genes identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in a particular embodiment, the polypeptide encoded by the gene identified herein or the drug candidate is in a solution phase, e. g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachments are formed by coating the solid surface with a solution of the polypeptide and drying. Alternatively, an immobilized monoclonal antibody, specific for the polypeptide to be immobilized can be used to anchor it to a solid surface. This is performed by adding the non-immobilized component, which may be labeled by a detectable label, e. g., the coated surface containing the anchored component. When the reaction is complete, the component is removed, e. g., by washing, and complexes anchored on the solid surface are detected. When the component carries a detectable label, the detection of label immobilized on the surface indicates the presence of the originally non-immobilized component. The detection of a label, complexing can be detected, for example, by an antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular protein encoded by a gene identified herein, interaction with that protein can be assayed by methods well known for detecting protein-protein interactions. Traditional approaches, such as, cross-linking, co-immunoprecipitation, and co-purification through ion exchange columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic screen and co-workers [Fields and Song, *Nature* (London) 340,245-246 (1989); Chien et al., *Proc. Natl. Acad. Sci. USA* 88,9578-9582 (1991)] as disclosed by Chevray and Nathans, *Proc. Natl. Acad. Sci. USA* 89,5805-5809 (1992).

Transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, a DNA-binding domain, while the other one functioning as the transcription activation domain. The yeast expression system (generally referred to as the "two-hybrid system") takes advantage of this property of these proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another protein is fused to the activation domain. The expression of a GAL1-lacZ reporter gene under control of the promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing the reporter gene will produce a blue color, while colonies lacking the reporter gene will be white.

are detected with a chromogenic substrate for  $\beta$ -galactosidase. A complete kit (MATCHMAKE) is available for mapping interactions between two specific proteins using the two-hybrid technique. This technique is commercially available and can also be extended to map protein domains involved in specific protein interactions as well as to identify those interactions that are crucial for these interactions.

In order to find compounds that interfere with the interaction of a gene identified herein and other components, a reaction mixture can be tested, a reaction mixture is usually prepared containing the product of the gene of interest under conditions and for a time allowing for the interaction and binding of the two proteins. A third compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. The binding of the test compound may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) of the test compound and the intra- or extracellular component present in the mixture is monitored as described.

The formation of a complex in the control reaction (s) but not in the reaction mixture containing the test compound interferes with the interaction of the test compound and its reaction partner.

K. Compositions and Methods for the Treatment of Psoriasis The compositions useful in the treatment of psoriasis, without limitation, proteins, antibodies, small organic molecules, peptides, phosphopeptides, arabinoside, and triple helix molecules, etc. that inhibit immune function, for example, T cell proliferation/activation, and cell infiltration.

For example, antisense RNA and RNA molecules act to directly block the translation of mRNA and preventing protein translation. When antisense DNA is used, oligodeoxyribonucleotides deoxyribose, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA.

Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques (e.g., Rossi, Current Biology 4, 469-471 (1994), and PCT publication No. WO 97/33551 (published 1997)).

Nucleic acid molecules in triple helix formation used to inhibit transcription should be single-stranded deoxynucleotides. The base composition of these oligonucleotides is designed such that it prior to the cleavage site. Hoogsteen base pairing rules, which generally require sizeable stretches of purines or pyrimidines. Further details see, e.g., PCT publication No. WO 97/33551, supra.

These molecules can be identified by any or any combination of the screening assays discussed herein. Screening techniques well known for those skilled in the art.

L. Anti-PRO Antibodies The present invention further provides anti-PRO antibodies. Exemplary antibodies include monoclonal, humanized, bispecific, and heteroconjugate antibodies.

1. Polyclonal Antibodies The anti-PRO antibodies may comprise polyclonal antibodies. Methods for producing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example a mouse, by immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant are administered in multiple subcutaneous or intraperitoneal injections.

The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be used as an antigen to a protein known to be immunogenic in the mammal being immunized.

Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, is thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immun selected by one skilled in the art without undue experimentation.

2. Monoclonal Antibodies The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Mo prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256: 4; method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immuniz lymphocytes that produce or are capable of producing antibodies that will specifically bind to the imm the lymphocytes may be immunized in vitro.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof.

Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclon and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed fr myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are em; may be cultured in a suitable culture medium that preferably contains one or more substances that in the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine gua transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxan thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression antibody-producing cells, and are sensitive to a medium such as HAT medium.

More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instanc Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Vir mouse-human heteromyeloma cell lines also have been described for the production of human mon Immunol., 133: 3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applic New York, (1987) pp.

51-63].

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the in by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclon example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107: 220

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution pro standard methods [Goding, supra]. Suitable culture media for this purpose include, for example, Dull Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown in vivo as ascites

The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture in conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hy chromatography, gel electrophoresis, dialysis, or affinity chromatography.



derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can selectively immobilize enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Med. 175: 217-225 (1992) describe the production of a fully humanized bispecific antibody F (ab')<sub>2</sub> Z which was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and not trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant DNA are described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al. 1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' antibody genes by gene fusion.

The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form heterodimers. This method can also be utilized for the production of antibody homodimers.

The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90: 6444-6448 (1993) is an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy chain connected to a light-chain variable domain (VL) by a linker which is too short to allow pairing between the two chains. Accordingly, the VH and VL domains of one fragment are forced to pair with the complement of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibodies is the use of single-chain Fv (scFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152: 53-57 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be made. Immunol. 147: 60 (1991).

Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide hereinafter referred to as a PRO. A polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte surface (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32), FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. The PRO may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. The PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EDTA, DTPA, or DOTA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF) or fibrinogen.

5. Heteroconjugate Antibodies Heteroconjugate antibodies are also within the scope of the present invention. Antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been used to target immune system cells to unwanted cells [U. S. Patent No. 4,676, 980], and for treatment of HIV infection [U. S. Patent No. 4,676, 980]. It is contemplated that the antibodies may be prepared in vitro using known antibody chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed by forming a thioether bond. Examples of suitable reagents for this purpose include 4-mercaptobutyrimide and those disclosed, for example, in U. S. Patent No. 4,676, 980.

6. Effector Function Engineering It may be desirable to modify the antibody of the invention with residues to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residues may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibodies have improved internalization capability and/or increased complement-mediated cell killing and anti-tumor activity. See, for example, U. S. Patent No. 4,676, 980.

Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff et al 2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

7. Immunoconjugates The invention also pertains to immunoconjugates comprising an antibody conjugated to a toxin, such as a chemotherapeutic agent, toxin (e. g., an enzymatically active toxin of bacterial, fungal, plant or animal origin), or a radioactive isotope (i. e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described: toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragment exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alkaloids, dimeric proteins, plant lectins, and enzymes. Examples include 212Bi, 213Bi, 214Bi, 215Bi, 216Bi, 217Bi, 218Bi, 219Bi, 220Bi, 221Bi, 222Bi, 223Bi, 224Bi, 225Bi, 226Bi, 227Bi, 228Bi, 229Bi, 230Bi, 231Bi, 232Bi, 233Bi, 234Bi, 235Bi, 236Bi, 237Bi, 238Bi, 239Bi, 240Bi, 241Bi, 242Bi, 243Bi, 244Bi, 245Bi, 246Bi, 247Bi, 248Bi, 249Bi, 250Bi, 251Bi, 252Bi, 253Bi, 254Bi, 255Bi, 256Bi, 257Bi, 258Bi, 259Bi, 260Bi, 261Bi, 262Bi, 263Bi, 264Bi, 265Bi, 266Bi, 267Bi, 268Bi, 269Bi, 270Bi, 271Bi, 272Bi, 273Bi, 274Bi, 275Bi, 276Bi, 277Bi, 278Bi, 279Bi, 280Bi, 281Bi, 282Bi, 283Bi, 284Bi, 285Bi, 286Bi, 287Bi, 288Bi, 289Bi, 290Bi, 291Bi, 292Bi, 293Bi, 294Bi, 295Bi, 296Bi, 297Bi, 298Bi, 299Bi, 300Bi, 301Bi, 302Bi, 303Bi, 304Bi, 305Bi, 306Bi, 307Bi, 308Bi, 309Bi, 310Bi, 311Bi, 312Bi, 313Bi, 314Bi, 315Bi, 316Bi, 317Bi, 318Bi, 319Bi, 320Bi, 321Bi, 322Bi, 323Bi, 324Bi, 325Bi, 326Bi, 327Bi, 328Bi, 329Bi, 330Bi, 331Bi, 332Bi, 333Bi, 334Bi, 335Bi, 336Bi, 337Bi, 338Bi, 339Bi, 340Bi, 341Bi, 342Bi, 343Bi, 344Bi, 345Bi, 346Bi, 347Bi, 348Bi, 349Bi, 350Bi, 351Bi, 352Bi, 353Bi, 354Bi, 355Bi, 356Bi, 357Bi, 358Bi, 359Bi, 360Bi, 361Bi, 362Bi, 363Bi, 364Bi, 365Bi, 366Bi, 367Bi, 368Bi, 369Bi, 370Bi, 371Bi, 372Bi, 373Bi, 374Bi, 375Bi, 376Bi, 377Bi, 378Bi, 379Bi, 380Bi, 381Bi, 382Bi, 383Bi, 384Bi, 385Bi, 386Bi, 387Bi, 388Bi, 389Bi, 390Bi, 391Bi, 392Bi, 393Bi, 394Bi, 395Bi, 396Bi, 397Bi, 398Bi, 399Bi, 400Bi, 401Bi, 402Bi, 403Bi, 404Bi, 405Bi, 406Bi, 407Bi, 408Bi, 409Bi, 410Bi, 411Bi, 412Bi, 413Bi, 414Bi, 415Bi, 416Bi, 417Bi, 418Bi, 419Bi, 420Bi, 421Bi, 422Bi, 423Bi, 424Bi, 425Bi, 426Bi, 427Bi, 428Bi, 429Bi, 430Bi, 431Bi, 432Bi, 433Bi, 434Bi, 435Bi, 436Bi, 437Bi, 438Bi, 439Bi, 440Bi, 441Bi, 442Bi, 443Bi, 444Bi, 445Bi, 446Bi, 447Bi, 448Bi, 449Bi, 450Bi, 451Bi, 452Bi, 453Bi, 454Bi, 455Bi, 456Bi, 457Bi, 458Bi, 459Bi, 460Bi, 461Bi, 462Bi, 463Bi, 464Bi, 465Bi, 466Bi, 467Bi, 468Bi, 469Bi, 470Bi, 471Bi, 472Bi, 473Bi, 474Bi, 475Bi, 476Bi, 477Bi, 478Bi, 479Bi, 480Bi, 481Bi, 482Bi, 483Bi, 484Bi, 485Bi, 486Bi, 487Bi, 488Bi, 489Bi, 490Bi, 491Bi, 492Bi, 493Bi, 494Bi, 495Bi, 496Bi, 497Bi, 498Bi, 499Bi, 500Bi, 501Bi, 502Bi, 503Bi, 504Bi, 505Bi, 506Bi, 507Bi, 508Bi, 509Bi, 510Bi, 511Bi, 512Bi, 513Bi, 514Bi, 515Bi, 516Bi, 517Bi, 518Bi, 519Bi, 520Bi, 521Bi, 522Bi, 523Bi, 524Bi, 525Bi, 526Bi, 527Bi, 528Bi, 529Bi, 530Bi, 531Bi, 532Bi, 533Bi, 534Bi, 535Bi, 536Bi, 537Bi, 538Bi, 539Bi, 540Bi, 541Bi, 542Bi, 543Bi, 544Bi, 545Bi, 546Bi, 547Bi, 548Bi, 549Bi, 550Bi, 551Bi, 552Bi, 553Bi, 554Bi, 555Bi, 556Bi, 557Bi, 558Bi, 559Bi, 560Bi, 561Bi, 562Bi, 563Bi, 564Bi, 565Bi, 566Bi, 567Bi, 568Bi, 569Bi, 570Bi, 571Bi, 572Bi, 573Bi, 574Bi, 575Bi, 576Bi, 577Bi, 578Bi, 579Bi, 580Bi, 581Bi, 582Bi, 583Bi, 584Bi, 585Bi, 586Bi, 587Bi, 588Bi, 589Bi, 590Bi, 591Bi, 592Bi, 593Bi, 594Bi, 595Bi, 596Bi, 597Bi, 598Bi, 599Bi, 600Bi, 601Bi, 602Bi, 603Bi, 604Bi, 605Bi, 606Bi, 607Bi, 608Bi, 609Bi, 610Bi, 611Bi, 612Bi, 613Bi, 614Bi, 615Bi, 616Bi, 617Bi, 618Bi, 619Bi, 620Bi, 621Bi, 622Bi, 623Bi, 624Bi, 625Bi, 626Bi, 627Bi, 628Bi, 629Bi, 630Bi, 631Bi, 632Bi, 633Bi, 634Bi, 635Bi, 636Bi, 637Bi, 638Bi, 639Bi, 640Bi, 641Bi, 642Bi, 643Bi, 644Bi, 645Bi, 646Bi, 647Bi, 648Bi, 649Bi, 650Bi, 651Bi, 652Bi, 653Bi, 654Bi, 655Bi, 656Bi, 657Bi, 658Bi, 659Bi, 660Bi, 661Bi, 662Bi, 663Bi, 664Bi, 665Bi, 666Bi, 667Bi, 668Bi, 669Bi, 670Bi, 671Bi, 672Bi, 673Bi, 674Bi, 675Bi, 676Bi, 677Bi, 678Bi, 679Bi, 680Bi, 681Bi, 682Bi, 683Bi, 684Bi, 685Bi, 686Bi, 687Bi, 688Bi, 689Bi, 690Bi, 691Bi, 692Bi, 693Bi, 694Bi, 695Bi, 696Bi, 697Bi, 698Bi, 699Bi, 700Bi, 701Bi, 702Bi, 703Bi, 704Bi, 705Bi, 706Bi, 707Bi, 708Bi, 709Bi, 710Bi, 711Bi, 712Bi, 713Bi, 714Bi, 715Bi, 716Bi, 717Bi, 718Bi, 719Bi, 720Bi, 721Bi, 722Bi, 723Bi, 724Bi, 725Bi, 726Bi, 727Bi, 728Bi, 729Bi, 730Bi, 731Bi, 732Bi, 733Bi, 734Bi, 735Bi, 736Bi, 737Bi, 738Bi, 739Bi, 740Bi, 741Bi, 742Bi, 743Bi, 744Bi, 745Bi, 746Bi, 747Bi, 748Bi, 749Bi, 750Bi, 751Bi, 752Bi, 753Bi, 754Bi, 755Bi, 756Bi, 757Bi, 758Bi, 759Bi, 760Bi, 761Bi, 762Bi, 763Bi, 764Bi, 765Bi, 766Bi, 767Bi, 768Bi, 769Bi, 770Bi, 771Bi, 772Bi, 773Bi, 774Bi, 775Bi, 776Bi, 777Bi, 778Bi, 779Bi, 780Bi, 781Bi, 782Bi, 783Bi, 784Bi, 785Bi, 786Bi, 787Bi, 788Bi, 789Bi, 790Bi, 791Bi, 792Bi, 793Bi, 794Bi, 795Bi, 796Bi, 797Bi, 798Bi, 799Bi, 800Bi, 801Bi, 802Bi, 803Bi, 804Bi, 805Bi, 806Bi, 807Bi, 808Bi, 809Bi, 810Bi, 811Bi, 812Bi, 813Bi, 814Bi, 815Bi, 816Bi, 817Bi, 818Bi, 819Bi, 820Bi, 821Bi, 822Bi, 823Bi, 824Bi, 825Bi, 826Bi, 827Bi, 828Bi, 829Bi, 830Bi, 831Bi, 832Bi, 833Bi, 834Bi, 835Bi, 836Bi, 837Bi, 838Bi, 839Bi, 840Bi, 841Bi, 842Bi, 843Bi, 844Bi, 845Bi, 846Bi, 847Bi, 848Bi, 849Bi, 850Bi, 851Bi, 852Bi, 853Bi, 854Bi, 855Bi, 856Bi, 857Bi, 858Bi, 859Bi, 860Bi, 861Bi, 862Bi, 863Bi, 864Bi, 865Bi, 866Bi, 867Bi, 868Bi, 869Bi, 870Bi, 871Bi, 872Bi, 873Bi, 874Bi, 875Bi, 876Bi, 877Bi, 878Bi,

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling reagents. Examples of bifunctional reagents include: (1) succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of iminothiolane (IT), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde) (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazonium diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1, 5-diisocyanatobenzyl-3-methoxydiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelator. For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). isothiocyanatobenzyl-3-methoxydiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelator. radionucleotide to the antibody. See W094/11026.

In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound circulation using a clearing agent and then administration of a "ligand" (e. g. , avidin) that is conjugate a radionucleotide).

8. Immunoliposomes The antibodies disclosed herein may also be formulated as immunoliposomes. antibody are prepared by methods known in the art, such as described in Epstein et al., Proc.

Natl. Acad. Sci. USA, 82: 3688 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA, 77: 4030 (1980); and

Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S.

Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposor filters of defined pore size to yield liposomes with the desired diameter. Fab/fragments of the antibody be conjugated to the liposomes as described in Martin et al., J. Biol. Chem., 257: 286-288 (1982) via reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. National Cancer Inst., 81 (19): 1484 (1989).

M. Pharmaceutical Compositions The active PRO molecules of the invention (e. g., PRO polypeptides or variants of each) as well as other molecules identified by the screening assays disclosed above, c

Therapeutic formulations of the active PRO molecule, preferably a polypeptide or antibody of the storage by mixing the active molecule having the desired degree of purity with optional pharmace excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. [1980] ) formulations or aqueous solutions.

Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and conce buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid a (such as octadecyltrimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium cl phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resor and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such a immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-form sodium; metal complexes (e. g., Zn-protein complexes); and/or non-ionic surfactants such as TWI polyethylene glycol (PEG).

Compounds identified by the screening assays disclosed herein can be formulated in an analogo techniques well known in the art.

Lipofections or liposomes can also be used to deliver the PRO molecule into cells. Where antibod smallest inhibitory fragment which specifically binds to the binding domain of the target protein is upon the variable region sequences of an antibody, peptide molecules can be designed which re protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant Marasco et al., Proc.

Natl. Acad. Sci. USA 90,7889-7893 [1993] ).

The formulation herein may also contain more than one active compound as necessary for the pa preferably those with complementary activities that do not adversely affect each other. Alternative composition may comprise a cytotoxic agent, cytokine or growth inhibitory agent. Such molecules combination in amounts that are effective for the purpose intended.

The active PRO molecules may also be entrapped in microcapsules prepared, for example, by co interfacial polymerization, for example, hydroxymethylcellulose or gelatin- microcapsules and poly microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin r nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remin 16th edition, Osol, A. Ed. (1980).

The formulations to be used for in vivo administration must be sterile. This is readily accomplishet filtration membranes.

Sustained-release preparations of the PRO molecules may be prepared. Suitable examples of su include semipermeable matrices of solid hydrophobic polymers containing the antibody, which me articles, e. g., films, or microcapsules. Examples of sustained-release matrices include polyesters (2-hydroxyethyl-methacrylate), or poly (vinylalcohol) ), polylactides (U. S. Pat. No. 3,773, 919), co y-ethyl-L- glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid c LUPRON DEPOT (injectable microspheres composed of lactic acid-glycolic acid copolymer and le 1,3-bisphosphoglyceric acid. While polymers such as ethylene vinyl acetate and lactic acid-glycolic acid

for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated a for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond to interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic content, using appropriate additives, and developing specific polymer matrix compositions.

N. Methods of Treatment It is contemplated that the polypeptides, antibodies and other active compounds may be used to treat psoriasis and related conditions, such as T cell mediated diseases, including the infiltration of inflammatory cells into a tissue.

Spondyloarthropathies are a group of disorders with some common clinical features and the common expression of HLA-B27 gene product. The disorders include: ankylosing spondylitis, Reiter's syndrome associated with inflammatory bowel disease, spondylitis associated with psoriasis, juvenile onset spondylitis, undifferentiated spondyloarthropathy. Distinguishing features include sacroileitis with or without spondylitis, asymmetric arthritis; association with HLA-B27 (a serologically defined allele of the HLA-B locus of chromosome 6, and absence of autoantibodies associated with other rheumatoid disease. The cell-mediated induction of the disease is the CD8+ T lymphocyte, a cell which targets antigen presented by class II cells may react against the class I MHC allele HLA-B27 as if it were a foreign peptide expressed by the cell. It has been hypothesized that an epitope of HLA-B27 may mimic a bacterial or other microbial antigenic epitope + T cells response.

Systemic sclerosis (scleroderma) has an unknown etiology. A hallmark of the disease is induration induced by an active inflammatory process. Scleroderma can be localized or systemic; vascular lesions of endothelial cell injury in the microvasculature is an early and important event in the development of systemic sclerosis. Vascular injury may be immune mediated. An immunologic basis is implied by the presence of monoclonal antibodies and the presence of anti-nuclear antibodies in many patients. ICAM-1 is often upregulated on endothelial cells in skin lesions suggesting that T cell interaction with these cells may have a role in the disease. Other organs involved include: the gastrointestinal tract: smooth muscle atrophy and fibrosis resulting in motility; kidney: concentric subendothelial intimal proliferation affecting small arcuate and interlobular arteries; reduced renal cortical blood flow, results in proteinuria, azotemia and hypertension; skeletal muscle: inflammation; lung: interstitial pneumonitis and interstitial fibrosis; and heart: contraction band necrosis.

Autoimmune or Immune-mediated Skin Disease including Bullous Skin Diseases, Erythema Multiforme are mediated by auto-antibodies, the genesis of which is T lymphocyte-dependent.

Psoriasis is proposed to be a T lymphocyte-mediated inflammatory disease. Lesions contain infiltrates of macrophages and antigen processing cells, and some neutrophils.

Transplantation associated diseases, including Graft rejection and Graft-Versus-Host-Disease (GVHD) dependent; inhibition of T lymphocyte function is ameliorative.

The compounds of the present invention, e.g., polypeptides or antibodies, are administered to a mammal in accordance with known methods, such as intravenous administration as a bolus or by continuous infusion intramuscular, intraperitoneal, intracerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, inhalation (intranasal, intrapulmonary) routes. Intravenous or inhaled administration of polypeptides or antibodies is contemplated.

In immunoadjuvant therapy, other therapeutic regimens, such as administration of an anti-cancer agent or administration of the proteins, antibodies or compounds of the present invention. For example, the compounds of the present invention may be administered in combination with other therapeutic agents.



immunoadjuvant of the invention may also receive an anti-cancer agent (chemotherapeutic agent). Preparation and dosing schedules for such chemotherapeutic agents may be used according to determined empirically by the skilled practitioner. Preparation and dosing schedules for such chemotherapeutic agents are described in M. C. Perry, Williams & Wilkins, Baltimore, MD (1992).

The chemotherapeutic agent may precede, or follow administration of the immunoadjuvant or may be administered therewith. Additionally, an anti-estrogen compound such as tamoxifen or an anti-progesterone (e.g., RU-38476) may be given in dosages known for such molecules.

It may be desirable to also administer antibodies against other immune disease associated or to antibodies which bind to CD20, CD18, CD11a, CD11b, CD11c, CD11d, CD11e, CD11f, CD11g, CD11h, CD11i, CD11j, CD11k, CD11l, CD11m, CD11n, CD11o, CD11p, CD11q, CD11r, CD11s, CD11t, CD11u, CD11v, CD11w, CD11x, CD11y, CD11z, CD11aa, CD11ab, CD11ac, CD11ad, CD11ae, CD11af, CD11ag, CD11ah, CD11ai, CD11aj, CD11ak, CD11al, CD11am, CD11an, CD11ao, CD11ap, CD11aq, CD11ar, CD11as, CD11at, CD11au, CD11av, CD11aw, CD11ax, CD11ay, CD11az, CD11ba, CD11bb, CD11bc, CD11bd, CD11be, CD11bf, CD11bg, CD11bh, CD11bi, CD11bj, CD11bk, CD11bl, CD11bm, CD11bn, CD11bo, CD11bp, CD11bq, CD11br, CD11bs, CD11bt, CD11bu, CD11bv, CD11bw, CD11bx, CD11by, CD11bz, CD11ca, CD11cb, CD11cc, CD11cd, CD11ce, CD11cf, CD11cg, CD11ch, CD11ci, CD11cj, CD11ck, CD11cl, CD11cm, CD11cn, CD11co, CD11cp, CD11cq, CD11cr, CD11cs, CD11ct, CD11cu, CD11cv, CD11cw, CD11cx, CD11cy, CD11cz, CD11da, CD11db, CD11dc, CD11dd, CD11de, CD11df, CD11dg, CD11dh, CD11di, CD11dj, CD11dk, CD11dl, CD11dm, CD11dn, CD11do, CD11dp, CD11dq, CD11dr, CD11ds, CD11dt, CD11du, CD11dv, CD11dw, CD11dx, CD11dy, CD11dz, CD11ea, CD11eb, CD11ec, CD11ed, CD11ee, CD11ef, CD11eg, CD11eh, CD11ei, CD11ej, CD11ek, CD11el, CD11em, CD11en, CD11eo, CD11ep, CD11eq, CD11er, CD11es, CD11et, CD11eu, CD11ev, CD11ew, CD11ex, CD11ey, CD11ez, CD11fa, CD11fb, CD11fc, CD11fd, CD11fe, CD11ff, CD11fg, CD11fh, CD11fi, CD11fj, CD11fk, CD11fl, CD11fm, CD11fn, CD11fo, CD11fp, CD11fq, CD11fr, CD11fs, CD11ft, CD11fu, CD11fv, CD11fw, CD11fx, CD11fy, CD11fz, CD11ga, CD11gb, CD11gc, CD11gd, CD11ge, CD11gf, CD11gg, CD11gh, CD11gi, CD11gj, CD11gk, CD11gl, CD11gm, CD11gn, CD11go, CD11gp, CD11gq, CD11gr, CD11gs, CD11gt, CD11gu, CD11gv, CD11gw, CD11gx, CD11gy, CD11gz, CD11ha, CD11hb, CD11hc, CD11hd, CD11he, CD11hf, CD11hg, CD11hi, CD11hj, CD11hk, CD11hl, CD11hm, CD11hn, CD11ho, CD11hp, CD11hq, CD11hr, CD11hs, CD11ht, CD11hu, CD11hv, CD11hw, CD11hx, CD11hy, CD11hz, CD11ia, CD11ib, CD11ic, CD11id, CD11ie, CD11if, CD11ig, CD11ih, CD11ii, CD11ij, CD11ik, CD11il, CD11im, CD11in, CD11io, CD11ip, CD11iq, CD11ir, CD11is, CD11it, CD11iu, CD11iv, CD11iw, CD11ix, CD11iy, CD11iz, CD11ja, CD11jb, CD11jc, CD11jd, CD11je, CD11jf, CD11jg, CD11jh, CD11ji, CD11jj, CD11jk, CD11jl, CD11jm, CD11jn, CD11jo, CD11jp, CD11jq, CD11jr, CD11js, CD11jt, CD11ju, CD11jv, CD11jw, CD11jx, CD11jy, CD11jz, CD11ka, CD11kb, CD11kc, CD11kd, CD11ke, CD11kf, CD11kg, CD11kh, CD11ki, CD11kj, CD11kk, CD11kl, CD11km, CD11kn, CD11ko, CD11kp, CD11kq, CD11kr, CD11ks, CD11kt, CD11ku, CD11kv, CD11kw, CD11kx, CD11ky, CD11kz, CD11la, CD11lb, CD11lc, CD11ld, CD11le, CD11lf, CD11lg, CD11lh, CD11li, CD11lj, CD11lk, CD11ll, CD11lm, CD11ln, CD11lo, CD11lp, CD11lq, CD11lr, CD11ls, CD11lt, CD11lu, CD11lv, CD11lw, CD11lx, CD11ly, CD11lz, CD11ma, CD11mb, CD11mc, CD11md, CD11me, CD11mf, CD11mg, CD11mh, CD11mi, CD11mj, CD11mk, CD11ml, CD11mm, CD11mn, CD11mo, CD11mp, CD11mq, CD11mr, CD11ms, CD11mt, CD11mu, CD11mv, CD11mw, CD11mx, CD11my, CD11mz, CD11na, CD11nb, CD11nc, CD11nd, CD11ne, CD11nf, CD11ng, CD11nh, CD11ni, CD11nj, CD11nk, CD11nl, CD11nm, CD11nn, CD11no, CD11np, CD11nq, CD11nr, CD11ns, CD11nt, CD11nu, CD11nv, CD11nw, CD11nx, CD11ny, CD11nz, CD11oa, CD11ob, CD11oc, CD11od, CD11oe, CD11of, CD11og, CD11oh, CD11oi, CD11oj, CD11ok, CD11ol, CD11om, CD11on, CD11oo, CD11op, CD11oq, CD11or, CD11os, CD11ot, CD11ou, CD11ov, CD11ow, CD11ox, CD11oy, CD11oz, CD11pa, CD11pb, CD11pc, CD11pd, CD11pe, CD11pf, CD11pg, CD11ph, CD11pi, CD11pj, CD11pk, CD11pl, CD11pm, CD11pn, CD11po, CD11pp, CD11pq, CD11pr, CD11ps, CD11pt, CD11pu, CD11pv, CD11pw, CD11px, CD11py, CD11pz, CD11qa, CD11qb, CD11qc, CD11qd, CD11qe, CD11qf, CD11qg, CD11qh, CD11qi, CD11qj, CD11qk, CD11ql, CD11qm, CD11qn, CD11qo, CD11qp, CD11qq, CD11qr, CD11qs, CD11qt, CD11qu, CD11qv, CD11qw, CD11qx, CD11qy, CD11qz, CD11ra, CD11rb, CD11rc, CD11rd, CD11re, CD11rf, CD11rg, CD11rh, CD11ri, CD11rj, CD11rk, CD11rl, CD11rm, CD11rn, CD11ro, CD11rp, CD11rq, CD11rr, CD11rs, CD11rt, CD11ru, CD11rv, CD11rw, CD11rx, CD11ry, CD11rz, CD11sa, CD11sb, CD11sc, CD11sd, CD11se, CD11sf, CD11sg, CD11sh, CD11si, CD11sj, CD11sk, CD11sl, CD11sm, CD11sn, CD11so, CD11sp, CD11sq, CD11sr, CD11ss, CD11st, CD11su, CD11sv, CD11sw, CD11sx, CD11sy, CD11sz, CD11ta, CD11tb, CD11tc, CD11td, CD11te, CD11tf, CD11tg, CD11th, CD11ti, CD11tj, CD11tk, CD11tl, CD11tm, CD11tn, CD11to, CD11tp, CD11tq, CD11tr, CD11ts, CD11tt, CD11tu, CD11tv, CD11tw, CD11tx, CD11ty, CD11tz, CD11ua, CD11ub, CD11uc, CD11ud, CD11ue, CD11uf, CD11ug, CD11uh, CD11ui, CD11uj, CD11uk, CD11ul, CD11um, CD11un, CD11uo, CD11up, CD11uq, CD11ur, CD11us, CD11ut, CD11uu, CD11uv, CD11uw, CD11ux, CD11uy, CD11uz, CD11va, CD11vb, CD11vc, CD11vd, CD11ve, CD11vf, CD11vg, CD11vh, CD11vi, CD11vj, CD11vk, CD11vl, CD11vm, CD11vn, CD11vo, CD11vp, CD11vq, CD11vr, CD11vs, CD11vt, CD11vu, CD11vv, CD11vw, CD11vx, CD11vy, CD11vz, CD11wa, CD11wb, CD11wc, CD11wd, CD11we, CD11wf, CD11wg, CD11wh, CD11wi, CD11wj, CD11wk, CD11wl, CD11wm, CD11wn, CD11wo, CD11wp, CD11wq, CD11wr, CD11ws, CD11wt, CD11wu, CD11wv, CD11ww, CD11wx, CD11wy, CD11wz, CD11xa, CD11xb, CD11xc, CD11xd, CD11xe, CD11xf, CD11xg, CD11xh, CD11xi, CD11xj, CD11xk, CD11xl, CD11xm, CD11xn, CD11xo, CD11xp, CD11xq, CD11xr, CD11xs, CD11xt, CD11xu, CD11xv, CD11xw, CD11xx, CD11xy, CD11xz, CD11ya, CD11yb, CD11yc, CD11yd, CD11ye, CD11yf, CD11yg, CD11yh, CD11yi, CD11yj, CD11yk, CD11yl, CD11ym, CD11yn, CD11yo, CD11yp, CD11yq, CD11yr, CD11ys, CD11yt, CD11yu, CD11yv, CD11yw, CD11yx, CD11yy, CD11yz, CD11za, CD11zb, CD11zc, CD11zd, CD11ze, CD11zf, CD11zg, CD11zh, CD11zi, CD11zj, CD11zk, CD11zl, CD11zm, CD11zn, CD11zo, CD11zp, CD11zq, CD11zr, CD11zs, CD11zt, CD11zu, CD11zv, CD11zw, CD11zx, CD11zy, CD11zz.

For the treatment or reduction in the severity of immune related disease, the appropriate dosage of the invention will depend on the type of disease to be treated, as defined above, the severity and course of the disease, the age of the patient, the patient's clinical history, the patient's clinical condition, and the discretion of the attending physician. The compound is suitably administered in a series of treatments.

For example, depending on the type and severity of the disease, about 1 mg/kg to 15 mg/kg (e.g., 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 7 mg/kg, 8 mg/kg, 9 mg/kg, 10 mg/kg, 11 mg/kg, 12 mg/kg, 13 mg/kg, 14 mg/kg, 15 mg/kg) of the compound may be administered to the patient, whether, for example, by intravenous administration, or by continuous infusion. A typical daily dosage might range from about 1 mg/kg to 15 mg/kg depending on the factors mentioned above.

For repeated administrations over several days or longer, depending on the condition, the treatment of disease symptoms occurs. However, other dosage regimens may be useful. The treatment may be monitored by conventional techniques and assays.

O. Articles of Manufacture In another embodiment of the invention, an article of manufacture comprising a PRO molecule) useful for the diagnosis or treatment of the disorders described above, the article of manufacture comprises a container and an instruction. Suitable containers include, for example, vials, ampoules, syringes, and the like. The containers may be formed from a variety of materials such as glass or plastic. The container is effective for diagnosing or treating the condition and may have a sterile access port (for example, a stopper pierceable by a hypodermic injection needle). The container may be a vial having a stopper pierceable by a hypodermic injection needle. The composition is usually a polypeptide or an antibody of the invention. An instruction or label on, or attached to, the container indicates that the composition is used for diagnosing or treating the condition of choice. The article of manufacture may comprise a second container comprising a pharmaceutically-acceptable buffer, such as phosphate buffered saline (PBS), dextrose solution, and the like. It may further include other materials desirable from a commercial standpoint, such as other buffers, diluents, filters, needles, syringes, and package inserts with instructions for use.

P. Diagnosis and Prognosis of Immune Related Disease Cell surface proteins, such as proteins of the immune system, are excellent targets for drug candidates or disease treatment. The same proteins also by the genes amplified in psoriasis find additional use in the diagnosis and prognosis of this disease. Directed against the protein products of genes amplified in psoriasis, can be used as diagnostics or

For example, antibodies, including antibody fragments, can be proteins encoded by amplified or overexpressed genes ("mark detectable, e. g. , fluorescent label, and binding can be monitored by techniques known in the art. These techniques are particularly suitable for binding assays are performed essentially as described above.

iii) In situ detection of antibody binding to the marker gene product by immunoelectron microscopy. For this purpose, a histological section is applied to it, preferably by overlaying the antibody on a biological distribution of the marker gene product in the tissue examined. histological methods are readily available for in situ detection.

The following examples are offered for illustrative purposes on any way.

All patent and literature references cited in the present specification

EXAMPLES Commercially available reagents referred to in the specification unless otherwise indicated. The source of those cells identified by ATCC accession numbers is the American Type Culture Collection.

EXAMPLE 1: Microarray analysis of PRO in Psoriasis Skin biopsies. "normal skin") were obtained. For each psoriatic patient, skin biopsies were obtained. The skin biopsies were differentially expressed, analyzed for Keratin6 staining via immunohistochemistry and used for RNA isolation. The skin biopsies were homogenized in 600 µl RNeasy Mini columns (Qiagen) with on-column DNase treatment. RNA isolation, RNA was quantitated using RiboGreen™ (Molecular Biology) agarose gels for integrity. The RNA yields ranged from 19 to 50 µg for matched control skin and 5. 4 to 10 µg for normal skin. zipped RNA of RNA proprietary Genentech microarray and Affymetrix microarrays were downregulated in psoriatic skin vs non-lesional skin, thus compared the same patient, and also comparing against normal skin biopsies. of this experiment is that the nucleic acids and encoded proteins of lesional skin in comparison to matched non-lesional skin from psoriasis. The nucleic acids and encoded proteins of Figure 13: Figure 853, Figure 1004, Figure 1283, Figure 1730, Figure 1804, lesional skin compared to matched non-lesional skin from psoriasis.

EXAMPLE 2: Use of PRO as a hybridization probe. The following examples are offered for illustrative purposes on any way as a hybridization probe.

DNA comprising the coding sequence of full-length or mature forms of homologous DNAs (such as those encoding naturally-occurring proteins) genomic libraries.

Hybridization and washing of filters containing either library DNA

Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, a 10% solution of salmon sperm DNA, and 50% formamide. The filters are washed in 2x SSC at 65°C for 15 minutes. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% S

DNA having a desired sequence identity with the DNA encoding full-length native sequence. Standard techniques known in the art.

**EXAMPLE 3: Expression of PRO in E. coli** This example illustrates preparation of an unglycosylated PRO in E. coli.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primer sites which correspond to the restriction enzyme sites on the selected expression vector may be employed. An example of a suitable vector is pBR322 (derived from E. coli; see B) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzymes to remove the antibiotic resistance genes and then ligated into the vector. The vector will preferably include an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected E. coli strain using the methods described in the art. Transformants are identified by their ability to grow on LB plates and antibiotic resistance can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplier which may subsequently be used to inoculate a larger scale culture. The cells are then grown in which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation and the supernatant can be solubilized using various agents known in the art, and the solubilized protein can be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in E. coli in a poly-His tagged form, using the following procedure. The PRO is amplified using selected PCR primers. The primers will contain restriction enzyme sites with enzyme sites on the selected expression vector, and other useful sequences providing for initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The sequences are then ligated into an expression vector, which is used to transform a strain of E. coli (W3110 fhuA (tonA) lon galE proHTs (htpRts) clpP (lacIq)). Transformants are first grown in LB broth at 30°C with shaking until an O.D. 600 of 3-5 is reached. Cultures are then diluted 50-100 fold into a mixture of 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate-2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, as well as 110 mM MOPS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO<sub>4</sub> and incubated at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the cells are pelleted. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6x10<sup>9</sup> g pellets) is resuspended in 10 volumes (v/v) of buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1% and 0.1% respectively. The solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues reduced. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is then loaded onto a 5 ml Q-Sepharose ion exchange column (BioLing, 1 liter grade) and washed with additional buffer containing 50 mM imidazole (Calbiochem, 1 liter grade) and 7

containing 250 mM imidazole.

Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are calculated so that the concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 24 hours. The reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). The protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA in water with a gradient of acetonitrile from 10 to 80%.

Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing the desired protein are pooled. Generally, the properly refolded species of most proteins are eluted at 10-20% acetonitrile since those species are the most compact with their hydrophobic interiors shielded from the solvent. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition, some proteins from the desired form, the reversed phase step also removes endotoxin from the sample.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

**EXAMPLE 4: Expression of PRO in mammalian cells** This example illustrates preparation of a potential PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. The vector is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, antibiotics. About 10<sup>6</sup> cells of pRK5-PRO DNA is mixed with about 1 µg DNA encoding the VA RNA gene (GenBank accession number: 31: 543 (1982) ) and dissolved in 500 µl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl<sub>2</sub>. To this is added 50 µl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO<sub>4</sub>, and a precipitate is allowed to form. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The supernatant is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with a fresh culture medium containing 200 IIC/ml 35S-cysteine and 200 IIC/ml 35S-methionine. After a 12 hour period, the medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel is then exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures contain undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran <Br>method described by Sambrook et al. (Mol. Cell. Biol. 9: 7575-7584, 1989).

spinner flask and 700  $\mu$ g pRK5-PRO DNA is added. The cells are first conc washed with PBS. The DNA-dextran precipitate is incubated on the cell pel glycerol for 90 seconds, washed with tissue culture medium, and re-introdu medium, 5 u. g/ml bovine insulin and 0.1 gel bovine transferrin. After about filtered to remove cells and debris. The sample containing expressed PRO method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-P reagents such as CaPO<sub>4</sub> or DEAE-dextran. As described above, the cell cl with culture medium (alone) or medium containing a radiolabel such as <sup>35</sup>S polypeptide, the culture medium may be replaced with serum free medium. days, and then the conditioned medium is harvested. The medium containi purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO r subclone insert can undergo PCR to fuse in frame with a selected epitope t vector. The poly-his tagged PRO insert can then be subcloned into a SV40 selection marker such as DHFR for selection of stable clones. Finally, the C the SV40 promoter/enhancer containing vector. Labeling may be performed

The culture medium containing the expressed poly-His tagged PRO can the method, such as by Ni<sup>2+</sup>-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expre expression procedure.

Stable expression in CHO cells is performed using the following procedure. (immunoadhesin), in which the coding sequences for the soluble forms (e. fused to an IgG1 constant region sequence containing the hinge, CH2 and

Following PCR amplification, the respective DNAs are subcloned in a CHO techniques as described in Ausubel et al. , Current Protocols of Molecular E expression vectors are constructed to have compatible restriction sites 5' at shuttling of cDNA's. The vector used expression in CHO cells is as describ (1996), and uses the SV40 early promoter/enhancer to drive expression of (DHFR). DHFR expression permits selection for stable maintenance of the

Twelve micrograms of the desired plasmid DNA is introduced into approxin available transfection reagents SuperfectO (Qiagen), Doser&commat; or F as described in Lucas et al., supra. Approximately 3 x 10<sup>-7</sup> cells are frozen described below.

The ampules containing the plasmid DNA are thawed by placement into wa pipetted into a centrifuge tube containing 10 mL of media and centrifuged a and the cells are resuspended in 10 mL of selective media (0.2  $\mu$ m filtered The cells are then aliquoted into a 100 mL spinner containing 90 mL of sele into a 250 mL spinner filled with 150 mL selective growth medium and incul and 2000 mL spinners are seeded with 3 x 10<sup>5</sup> cells/mL. The cell media is resuspension in production medium. Although any suitable CHO media ma

S. Patent No. 5,122, 469, issued June 16, 1992 may actually be used. A 3L p day 0, pH is determined. On day 1, the spinner is sampled and sparging with sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) t as necessary to keep it at around 7.2. After 10 days, or until the viability drop centrifugation and filtering through a 0.22  $\mu$ m filter.

The filtrate was either stored at 4°C or immediately loaded onto columns for i

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA c

Before purification, imidazole is added to the conditioned media to a concentratio onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer containing 0.25 M imidazole. The highly purified protein is containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 mM 80°C.

Immunoaffinity (Fc-containing) constructs are purified from the conditioned media pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated with loading, the column is washed extensively with equilibration buffer before elution. protein is immediately neutralized by collecting 1 ml fractions into tubes containing purified protein is subsequently desalted into storage buffer as described above. homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino

Many of the PRO polypeptides disclosed herein were successfully expressed

EXAMPLE 5: Expression of PRO in Yeast The following method describes re

First, yeast expression vectors are constructed for intracellular production of DNA encoding PRO and the promoter is inserted into suitable restriction enzyme intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other  $\alpha$ -factor or invertase secretory signal/leader sequence, and linker sequence

Yeast cells, such as yeast strain AB 110, can then be transformed with the expression selected fermentation media. The transformed yeast supernatants can be analyzed and separation by SDS-PAGE, followed by staining of the gels with Coomassie

Recombinant PRO can subsequently be isolated and purified by removing the centrifugation and then concentrating the medium using selected cartridge filters

The concentrate containing PRO may further be purified using selected color

Many of the PRO polypeptides disclosed herein were successfully expressed

EXAMPLE 6: Expression of PRO in Baculovirus-Infected Insect Cells The following

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus. Tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular protein or the sequence encoding the mature protein if the protein is extracellular is amplified to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme site those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold<sup>®</sup> *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available of incubation at 28°C, the released viruses are harvested and used for further amplifications. <sup>1</sup> are performed as described by O'Reilly et al., Baculovirus expression vectors: A Laboratory Manual Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography. Cells are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 338, 852 (1990). Cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 1.0 M NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation and diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of water and equilibrated with 25 mL of loading buffer.

The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed with buffer, at which point fraction collection is started. Next, the column is washed with a secondary buffer (300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching the secondary buffer is developed with a 0 to 500 mM imidazole gradient in the secondary wash buffer. One mL fractions are collected by SDS-PAGE and silver staining or Western blot with Ni<sup>2+</sup>-NTA-conjugated to alkaline phosphatase.

Fractions containing the eluted Hisio-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known techniques including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

**EXAMPLE 7: Preparation of Antibodies that Bind PRO** This example illustrates preparation of antibodies that specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for example, in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1988. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant subcutaneously or intraperitoneally in an amount from 1-100 micrograms.

Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research Corporation, 13800 Via Arroyo, Poway, CA 92121). The immunized mice are then bled at 40 to 60 days post-immunization.

in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA for PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a suspension of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested, fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positivity" of the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks and the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation and exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to PRO is employed.

**EXAMPLE 8: Purification of PRO Polypeptides Using Specific Antibodies** Native or recombinant PRO is purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by immunoaffinity chromatography. For example, monoclonal anti-PRO polypeptide can be prepared by immunizing a mouse with recombinant PRO polypeptide. Alternatively, mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Alternatively, immunoglobulin is covalently attached to a chromatographic resin such as CNBr-activated Sepharose (Pharmacia Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is used according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction of the whole cell or of a soluble fraction of the whole cell. This preparation is derived by solubilization of the whole cell or of a soluble fraction of the whole cell by the addition of detergent or by other methods well known in the art. After differential centrifugation by the addition of detergent or by other methods well known in the art, the polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffer, high pH, high salt, etc.) are used to elute the polypeptide. Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and the polypeptide is collected.

**EXAMPLE 9: Drug Screening** This invention is particularly useful for screening compounds by using a method of screening compounds by using a fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment thereof can be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. Screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant DNA containing the PRO polypeptide or fragment thereof.



Drugs are screened against such transformed cells in competitive binding assays. Such cells, e used for standard binding assays. One may measure, for example, the formation of complexes fragment and the agent being tested. Alternatively, one can examine the diminution in complex polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which associated disease or disorder. These methods comprise contacting such an agent with an PRO and assaying (1) for the presence of a complex between the agent and the PRO polypeptide or a complex between the PRO polypeptide or fragment and the cell, by methods well known in the assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO separated from that present in bound form, and the amount of free or uncomplexed label is a particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly, small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. If detected by methods well known in the art. Purified PRO polypeptide can also be coated directly on a solid support. In addition, non-neutralizing antibodies can be used to immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralized PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments. The antibodies can be used to detect the presence of any peptide which shares one or more antigenic epitopes with the PRO polypeptide.

**EXAMPLE 10: Rational Drug Design** The goal of rational drug design is to produce structural analogs of a polypeptide of interest (i. e., a PRO polypeptide) or of small molecules with which they interact, inhibitors. Any of these examples can be used to fashion drugs which are more active or stable which enhance or interfere with the function of the PRO polypeptide *in vivo* (c. f., Hodgson, Biochem. J. 198, 1-10, 1981).

In one approach, the three-dimensional structure of the PRO polypeptide, or of a PRO polypeptide determined by x-ray crystallography, by computer modeling or, most typically, by a combination of shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and function of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be structure of homologous proteins. In both cases, relevant structural information is used to design molecules or to identify efficient inhibitors. Useful examples of rational drug design may include activity or stability as shown by Braxton and Wells, Biochemistry, 31: 7796-7801 (1992) or which antagonists of native peptides as shown by Athauda et al., J. Biochem., 113: 742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described by crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-id) to an active antibody. As a mirror image of a mirror image, the binding site of the anti-id would be expected to be complementary to the binding site of the original antibody. The anti-id could then be used to identify and isolate peptides from banks of cDNA libraries. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available for use in the above described methods.

studies as X-ray crystallography. In addition, guidance to those employing computer mode

The foregoing written specification is considered to be limited in scope by the illustration of certain aspects of the invention. The deposit of material herein does not constitute an admission that the practice of any aspect of the invention is inadequate to enable the practice of any aspect of the invention. The scope of the claims to the specific invention is limited by the scope of the claims to the specific invention. In addition to those shown and described herein, other embodiments of the invention will fall within the scope of the appended claims.